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APPOINTED BY

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FOREWORD

BY

SIR THOMAS LEWIS

The Cardiac Society of Great Britain and Ireland has decided that it is expedient for it to possess its own journal. The size of the society and the activity of many of its members render such a decision not only wise but inevitable.

There is no stronger tradition, concerning work upon the heart, than the British. Traced from the incomparable Harvey in the early part of the seventeenth century, through Richard Lower and Stephen Hales, the illustrious band of workers has been swollen by the great clinicians of the eighteenth and nineteenth centuries, Heberden, Parry, Withering, Corrigan, Hope, Stokes, Peacock, Ringer, Mackenzie, and by the great physiologists, Gaskell and Starling. All these names from the distant and recent past are linked with outstanding contributions to our knowledge of the heart and its maladies ; their work forms a legacy of great achievement. The members of the Cardiac Society of Great Britain and Ireland are the chief trustees of this legacy, and its weighty responsibility.

The success of the new journal will depend upon the quality and not primarily upon the quantity of the matter which it publishes. Originality of observation and of view will be the touchstone of quality. The work of editing is uncreative : an editor can publish only what is offered ; he will use most of what is offered. The journal's success is governed, therefore, from the source of the material. The best contributors will submit for publication only sound and original matter and thought. They will edit their own work ; will judge their own text impartially and will prune it ruthlessly, thinking of the standard of work accomplished and to be reported and not of personal interest ; they will prepare their manuscript in all particulars to save further labour ; they will facilitate the

reading by every device of conciseness, of simplicity, of clarity, and of accuracy, in composing text, figure explanation, and reference ; for every hour so spent by one who writes will save countless hours by the many who afterwards read. They will remember that the work of editing is a gratuitous and unenviable task, and they will bow loyally to editorial decision.

To express the hope that the new journal will come to possess many contributors of this kind is to give the fullest wishes for the journal's real and lasting success.

SOME DISTURBANCES OF THE RHYTHM OF THE HEART

BY

JOHN COWAN †

(From the Royal Infirmary, Glasgow)

I. INTRODUCTORY

The association of changes in the character of the pulse and serious cardiac symptoms was recognized many centuries ago, and carefully studied with all the means available at the time. But the significance of the arrhythmias has only been elucidated within the last few years, by the use of instrumental methods of analysis. In G. A. Gibson's text-book (1898), designed to be a mirror of the state of medical science and art at the close of the nineteenth century, only a couple of pages are devoted to the disturbances of the cardiac rhythm. James Mackenzie's book (1902) started an intensive study, and in his Morison Lectures, Gibson (1904) discussed paroxysmal tachycardia, extra-systole, and heart block. The study has continued, and our accumulated knowledge is now vastly greater than it was ten years ago, but there are still gaps on the clinical side. The following records are brought forward to augment the available data.

In the healthy individual each beat of the heart is occasioned by stimuli arising in the sino-auricular node, and spreading from it to the auricles and ventricles. The sinus pacemaker is under the control of the nervous system, and both the rhythm and the rate of the heart may be altered by nervous influences. "The heart responds to every emotion and sensation, and even thought, as well as to the demands created by muscular exertion or the organic processes such as digestion. . . . All states of the nervous system are reflected upon the circulation, each emotion being attended with its own reaction upon the heart and arteries, and even sensation producing recognizable results, so it is to be expected that diseases of the nervous system will be attended with special symptoms, manifested through the circulation, and by the pulse" (Broadbent, 1890). Stokes (1854) had previously referred to the influence of the nervous system upon the circulation, but he concluded that such disturbances of the pulse were more often related to functional disturbance rather than to organic disease of the nervous system, in contradistinction to disturb-

† Received June 15, 1938.

ances due to intrinsic cardiac causes, which were more often organic than functional.

Disturbances of the pulse may also arise from toxic causes, the activity of such poisons as digitalis or those of the infections ; though these doubtless act by their influence upon the nervous system or the heart itself.

In recent years attention has been largely focused upon the disturbances due to intrinsic cardiac causes ; those due to nervous and toxic causes have received little consideration. It is very important to recognize the nervous origin of an irregular pulse, for the mere suggestion of heart disease may cause incalculable mischief. We have all seen such cases. One came recently under my observation. I saw him first at the age of 13, when he gave a wonderful display of extrasystoles, clearly due to nervous causes. He was a big, healthy, growing schoolboy, who played all games with acceptance. He was advised to carry on ; but other advice was sought, and he was made an invalid. At the age of 27 he is an undersized, poorly developed, badly nourished hypochondriac. His heart still seems quite sound.

The present paper is mainly concerned with those disturbances of the cardiac rhythm which are due to causes *outwith* the heart.

The rhythm and the rate of the pulse in health are not absolutely regular. The rhythm, though apparently regular to the finger, is always irregular if accurately measured. During inspiration the rate is quickened and during expiration slowed. The rate of the pulse varies : fever may raise it to 120 per minute ; jaundice may lower it to 40 ; and comparable changes may occur from physical, psychical, or organic nervous influences. The variations are due to variations in the duration of diastole, the intrinsic mechanism of the heart continuing unchanged.

In health each beat of the heart is occasioned by stimuli arising in the sino-auricular node. Every part of the heart, however, possesses the inherent power of initiating stimuli, and the sino-auricular node only takes the lead because its rate of stimulus production (70-80 per minute) is more frequent than that elsewhere. The rate of the auriculo-ventricular node is 50-60 ; that of the ventricular muscle 20-30.

The heart may, at times, serve two masters. In many people stimuli occasionally arise elsewhere than in the sino-auricular node and cause a contraction : an extrasystole. If it concerns the ventricles alone, the normal sino-auricular rhythm of the auricles need not be disturbed, but an auricular extrasystole disturbs the sino-auricular rhythm for the moment.

If the rate set by the sino-auricular node becomes less than that set by the auriculo-ventricular node, the latter may take charge and cause a ventricular contraction. This may occur if the activity of the sino-auricular node is depressed so that its rate of stimulus production becomes less frequent than that of the auriculo-ventricular node. This can be caused, in experiment, by cooling the sino-auricular node ; by pressure upon the carotid sinus or the eyeballs ; by heavy doses of digitalis or quinidine. Cushny (1925) showed that in digitalis poisoning in animals, the rate of the auricular contractions

became less frequent and the irritability of the ventricles exaggerated, so that spontaneous contractions of the ventricles ensued, and, becoming more frequent, eventually established an "idio-ventricular rhythm," with a rate that might be equal to or more frequent than that of the auricles. The mechanism was clearly nervous, for if the vagus inhibition was put out of action by atropine the normal rhythm was restored.

The rate of stimulus production of the sino-auricular node may also become less frequent than that of the auriculo-ventricular node if the latter becomes hyper-irritable. This can be accomplished, in experiment, by warming the auriculo-ventricular node ; by the exhibition of atropine throwing the vagus nerve out of action ; by stimulation of the right vagus and left sympathetic nerves. In some cases more than one mechanism may be simultaneously in action.

As a rule, when the auriculo-ventricular node takes charge, the stimulus passes in a retrograde fashion to the auricles and causes an auricular contraction. In the case of an isolated auriculo-ventricular nodal extrasystole, this may not occur if the nodal stimulus reaches the auricle at a time when its muscle is refractory ; but if the stimuli are repeated the auricular rhythm is generally set by the auriculo-ventricular node (Nodal rhythm). In exceptional cases this retrograde conduction is disturbed, and the auricular contractions arise in response to stimuli originating in the sino-auricular node, while the ventricular contractions are in response to stimuli from the auriculo-ventricular node (Dissociation). But, curiously, in some cases where retrograde conduction is impeded the forward conduction of stimuli is not altogether inhibited, and at rare intervals the ventricles may respond to a sino-auricular stimulus flowing through the auricular muscle (Capture : dissociation with interference).

The majority of these cases are associated with an infrequent sinus rate and occur during the administration of digitalis ; but dissociation may occur apart from such drugging, the result of purely nervous causes.

The most frequent cause of dissociation is, of course, heart-block, due to damage to the auriculo-ventricular bundle, interrupting the passage of the stimuli from auricle to ventricle. The auricles continue to contract at the sinus rate, whatever it may be, while the ventricles contract infrequently, 20-30 times a minute. The pulse rate in heart-block is less frequent than in dissociation, for the ventricular contractions are due to stimuli arising in the muscle of the ventricle, and not, as in dissociation, in the auriculo-ventricular node. The interruption of the pathway between auricles and ventricles in full heart-block prevents the sino-auricular node from regaining control of the ventricular contractions even on occasion.

Heart-block is generally due to organic lesions in the tissues concerned, but may be of functional origin. It has been produced experimentally by digitalis and quinidine intoxication ; by vagal stimulation ; by asphyxia ; in anaphylactic reactions. It has been produced clinically by digitalis, and by pressure upon the carotid sinus or the eyeballs. If of functional origin it can

be removed by atropine; but if due to organic lesions atropine is inactive, and the ventricles pursue their slow rhythm uninfluenced by exertion, atropine, or vagal stimulation. An exception to this statement has been reported by Fleming and Stevenson (1928). A child, aged $3\frac{1}{2}$ years, with full heart-block and congenital heart disease, showed an increase in the auricular and the ventricular rates on the exhibition of atropine, although the block persisted unchanged.

The rate and the rhythm of the ventricular contractions may thus be affected by variations in the "tone" of the sino-auricular and the auriculo-ventricular nodes; and this may be due to functional or organic disturbances, depressing or exalting their particular functions. If the rate of the stimulus production in the two nodes is approximately similar, trifling alterations in rate of either may alter the rhythm for the time. Sinus irregularities, sino-auricular block, nodal rhythm, dissociation, extrasystoles may thus all occur, in quick succession or on separate occasions, in the same patient, as will appear in the following clinical records.

Disturbances of the rhythm of the heart may be due to intrinsic disorders of the heart or to causes arising outwith the organ. The prognosis and the treatment of the two groups vary according to the cause of the disturbance

II. ARRHYTHMIAS OF THE SINO-AURICULAR NODE

Sinus Arrhythmia.—Sinus irregularity of the pulse occurs most notably in children and young adults. The rate and the rhythm of the pulse are unstable. The intervals between the beats are variable, and diastole may be considerably prolonged (Fig. 1). The irregularity is often associated with the phases of

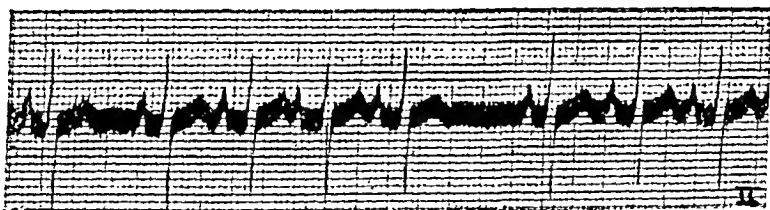


FIG. 1.—Sinus arrhythmia. The only abnormal feature is the varying length of diastole.
Lead II.

respiration, the rate quickening with inspiration and slowing with expiration. It is most distinct when the heart is beating slowly, and is lessened or abolished if the rate is increased, as, for instance, by exertion, or the administration of atropine. It can generally be influenced by voluntary changes in the respiratory rhythm, frequent, infrequent, or irregular breathing. The patients show active reflexes and are often highly strung.

It is rarely difficult to recognize sinus arrhythmia. Its relation to the respiratory phases and its disappearance with an increased pulse rate make its nature clear. The electrocardiogram shows variations in the duration of diastole and normal complexes.

Sinus arrhythmia is a physiological occurrence, and does not require any alteration of the usual habits of the individual, or any treatment.

Sino-Auricular Block : Type A, with Ventricular Standstill.—As already mentioned, the rhythm of the sino-auricular node is not perfectly regular. On occasion a sinus stimulus may default and the pulse misses a beat, neither auricle or ventricle contracting : sino-auricular block. The duration of the diastole is usually double that of the normal rhythm, but it may be somewhat shorter. Sometimes several beats in series may fail, and the standstill may last for several seconds.

Case A. Fig. 2 shows sino-auricular block. An active old man, aged 71, when stooping to pick up some papers, tumbled down unconscious. He recovered in a



FIG. 2.—Sino-auricular block ; type A. Case A. A single contraction of the heart fails. Lead I.

few moments, but his face was bruised and he stayed at home for a day or two before resuming work. A similar attack occurred a year later. Two months afterwards, in August, he was rather short of breath upon exertion, and he had a third syncope when out walking, but was able to return home. His pulse was now found, for the first time, to be infrequent and irregular. In September he looked healthy and active, but his lips were somewhat blue. The left heart was slightly enlarged ; the first sound was impure ; the second aortic sound emphatic. His pulse was regular, save for an occasional extrasystole, and infrequent, 30-40 per minute. The electrocardiogram showed dissociation with interference (see Fig. 14, p. 16).

The pulse rate remained unaltered for a fortnight, and then gradually rose, reaching normal figures (60-72) before the end of a month. In December he looked well, but did not feel inclined for much work. His pulse at first was regular, save for an occasional extrasystole, and numbered about 66. But while electrocardiograms were being taken pauses, of which he was unconscious, occurred between the cardiac contractions (Fig. 2). The standstills varied in duration. Sometimes a single beat failed, sometimes several. One standstill lasted for 3.3 seconds.

His subsequent life was short. On January 5 he felt bilious, and stayed in bed. He became drowsy on the 7th, the stupor deepened, and he died in coma on January 10. No paralysis was detected, but the pupils and the reflexes became unequal and the breathing of Cheyne-Stokes type. The pulse rate was unaltered, but the cardiac contractions ceased for a second or two at intervals. Eight pauses were recorded in a tracing during 123.5 seconds, and while *a. c.* and *v.* were clear with each beat in the jugulo-carotid curve the line was straight during the pauses.

The striking feature of his illness was the almost complete absence of symptoms of cardiac disability. The breathlessness experienced in August disappeared after two or three weeks and did not recur. There were never any signs of congestive failure. The end came with symptoms of cerebral character, and the sino-auricular block seemed due to a similar cause.

Case B. The patient was a lonely old bachelor, aged 54, who was seen for some trivial digestive disturbance. His organs seemed sound, but his pulse rate was infrequent, about 47 per minute, and irregular, a sinus irregularity with sino-auricular block (Fig. 3). His discomforts rapidly passed away. Two years later he complained

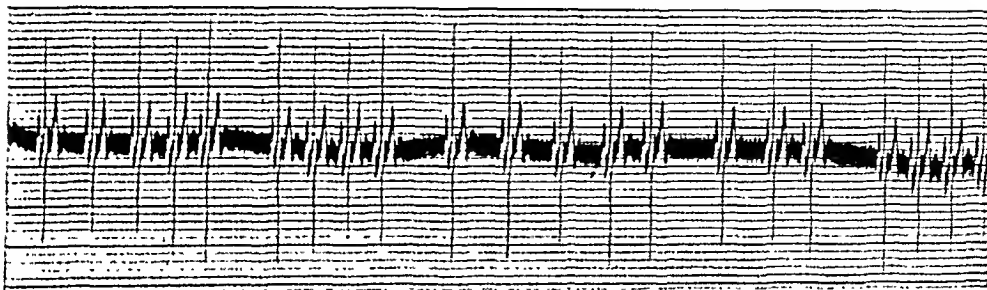


FIG. 3.—Sinus arrhythmia and sino-auricular block : type A. *Case B.* The record shows a series of progressively shortening auricular diastoles, leading up to long diastolic pauses. The disturbance of the auricular rhythm may be due to extreme sinus arrhythmia or to a sino-auricular block which displays features analogous to Wenckebach periods in auriculo-ventricular block. Lead II.

of his sense of taste ; his electrocardiogram showed an almost regular pulse of 43 per minute and normal complexes. Nine years later he is in good health. There was clearly a neurotic factor in all his complaints.

I can find few clinical records of cardiac standstill from sino-auricular block. Laslett's case (1908) is interesting, for the patient has now been under observation for nearly thirty years. A married woman, she enjoyed good health until the age of 36 (1904), when she became subject to syncopal attacks. In 1908 she was slightly anæmic and rather breathless on exertion. Some hæmic murmurs were audible on auscultation, but her organs otherwise seemed sound. The attacks recurred at intervals of three or four weeks, and were repeated for several days. The pulse, which usually was regular in rhythm and about 70 per minute, on these occasions became infrequent (30-40), as the heart often failed to contract, the result of sino-auricular block. If the standstill lasted for 4-5 seconds she lost consciousness, and if for longer the fingers might twitch. On one occasion she lost her speech for a week. Dr. Laslett courteously informs me (1937) that the attacks still recur as frequently as thirty years ago. She had a stroke two years ago, which has left her slightly aphasic and very decrepit, but she has never shown any signs of cardiac insufficiency. The rhythm of her heart is very sensitive to pressure upon the carotid sinus, and long pauses between the contractions are readily produced in this way.

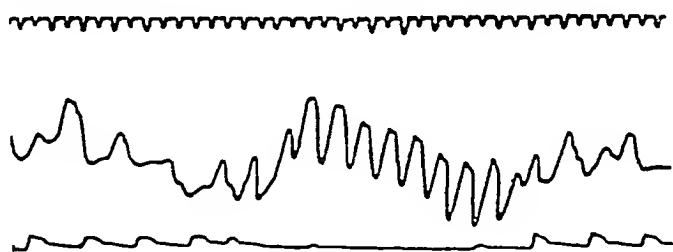
Heard and Strauss (1918) reported the case of a woman, aged 36, with tonsillitis and a dry pleurisy. She had been liable to "faints" since the age of 16. These attacks commenced with discomfort in the precordial region, and she became short of breath and cyanosed. On several occasions she lost consciousness. Attacks lasted for 15-60 minutes, and she felt weak for a day or two afterwards. They had become more frequent and more severe, and she had been an invalid for a year. She was undersized and nervous. The

Wassermann reaction was positive. Her uterus was undeveloped, but the other organs seemed sound. The pulse was very unstable, the rate, usually 40–70, varying between 40 and 126 per minute. On one occasion it ran 18–25 for a short period. The electrocardiogram showed a sinus arrhythmia and sino-auricular block. When she was under an anæsthetic, for curetting, the rhythm changed to an auriculo-ventricular nodal rhythm with a pulse rate of 83–97. Subsequently the rhythm became normal but later reverted to the original sinus irregularity.

Barlow (1927) reported several cases of sino-auricular block. A man, aged 65, who suffered from chronic arthritis, had an attack of giddiness one morning three years before he came under observation, with pain in the shoulder and breathlessness. His blood pressure was 190/90 mm., his heart was enlarged, and a systolic murmur was audible at the aortic cartilage. Sino-auricular block persisted for several months, but he had few discomforts. Another man, aged 41, complained of breathlessness, faintness, and exhaustion of two years' duration. His blood pressure was 140/70 mm., his heart of normal size, his mitral valve incompetent. The Wassermann reaction was positive. The electrocardiogram showed sino-auricular block. His condition remained unaltered for the next two years; and three years later he merely complained of lassitude although the block persisted.

In three of these cases syncopal attacks occurred on more than one occasion. The common causes of syncope are vaso-motor disturbances, and failure of the pulse from any cause, producing anæmia of the brain. If the failure is momentary the patient becomes pale; if it lasts for 4–5 seconds consciousness is lost; if for 10–12 seconds tonic or clonic convulsions supervene.

Attacks can be produced by pressure upon the carotid arteries. They occur in about one-third of the cases of heart-block most frequently at the period when the rhythm is changing from a partial to a complete block, and ventricular standstills occur from time to time. They are uncommon after full block has been established. I have recorded (1926) their occurrence in a case of paroxysmal nodal tachycardia, where the pulse failed during the paroxysms (Fig. 4).



P.R. 160

FIG. 4.—Polygraph tracing showing failure of the radial pulse during a short attack of nodal tachycardia. Case L, p. 19. P.R. 160.

Syncope may occur in sino-auricular block if the standstill is sufficiently

prolonged. The sequence was clearly proven in Laslett's case. The association of attacks of giddiness, faintness, and syncopes with periods of ventricular standstill in my case and that of Heard and Strauss suggest a similar origin ; but no attack occurred under observation.

Sino-Auricular Block : Type B.—When the sino-auricular stimulus is late in arriving and the auriculo-ventricular node supplies a stimulus for the ventricular contractions.

In this group of cases of sino-auricular block ventricular standstills do not persist for any length of time. On the failure of an auricular stimulus and the consequent prolongation of diastole, the inherent rhythmicity of the auriculo-ventricular node comes into action and evokes a ventricular beat (Fig. 5). As a rule the sinus node regains control of the ventricular contractions



FIG. 5.—Sino-auricular block : type B. Case C. Following the failure of a sinus stimulus and undue prolongation of diastole the auriculo-ventricular node sets the ventricular rhythm for one beat. Lead II.

after but one failure, but occasionally the auriculo-ventricular nodal rhythm continues for several cycles (Fig. 6). In some cases the change of rhythm recurs repeatedly in an irregular fashion.

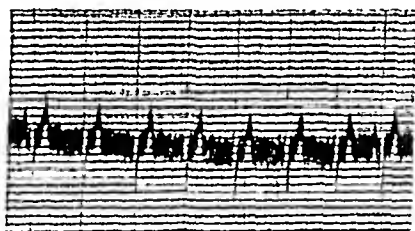


FIG. 6.—Sino-auricular block : type B. Case D. Following the failure of a sinus stimulus and undue prolongation of diastole the auriculo-ventricular node sets the ventricular rhythm for six beats. Lead II.

Case C. An active man, aged 57, had been liable to headaches, but otherwise had enjoyed good health until four years prior to his visit, when he became subject to indigestion and various muscular pains. He was thin and nervous, and looked older than his years. His organs seemed sound, but his pulse, numbering about 60 per minute, was very irregular. The electrocardiogram showed a fairly regular sino-auricular rhythm, with at times sino-auricular block : type B (Fig. 5).

His health improved though the irregularity persisted, and he continued at work for five years. At this time, after business worries, he had to enter a mental hospital, where he remained for four months. He was always eccentric in his habits and he had a family history of mental troubles. A year later he was seen again ; he looked stout and well, and only complained of slight breathlessness and discomfort in the chest upon exertion. His heart was larger than before and his blood pressure higher,

170/85 mm. Hg.; but there was little evidence of cardiac mischief. His pulse was infrequent, about 38 per minute, and very irregular as the pacemaker "wandered." In some records a fairly regular sinus rhythm continued for several beats, and was suddenly succeeded by a series of ventricular complexes without any evidence of auricular activity. On two occasions an inverted P was visible between RS and T (Fig. 7). In Fig. 8, taken just after Fig. 7, a positive P immediately preceded QRS

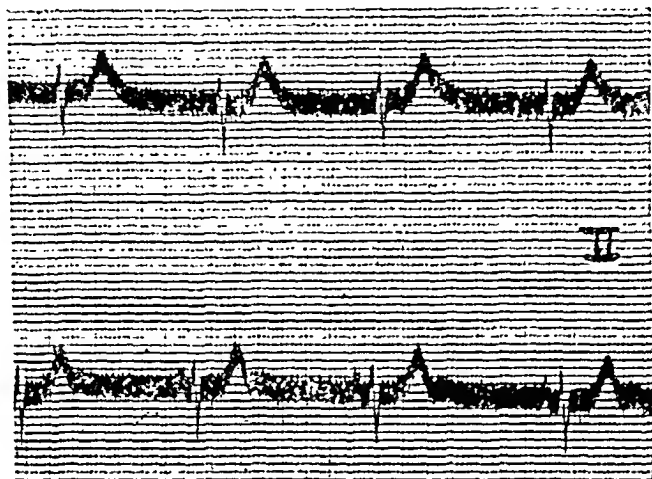


FIG. 7.—Sino-auricular block : type B. Case C. The upper record shows four beats of auriculo-ventricular nodal origin. An inverted P is visible between RS and T in the third complex. The lower record shows a return to sino-auricular control. Lead II.



FIG. 8.—Dissociation. Case C. The sinus rhythm is infrequent and irregular. The second auricular diastole is prolonged, and the auriculo-ventricular node, impatient at the delay of the auricular stimulus, sets the ventricular rhythm for the next three beats, after which the sinus rhythm becomes re-established. Lead II.

merging into the upstroke of R. The interpretation is difficult on account of the varying rate of the auricular contractions. The inverted P waves are evidently due to retrograde auricular activation, and their close proximity to QRS seems to preclude the possibility of P deflexions being buried in the other ventricular complexes. Probably the auricles were at rest save on these occasions : a high-grade sino-auricular block. The sinus rhythm in Fig. 8 is infrequent and irregular. The second auricular diastole is prolonged so the auriculo-ventricular node, impatient at the delay of the auricular stimulus, sets the ventricular rhythm for the next three beats (dissociation), after which the sinus rhythm becomes re-established.

The records are interesting as they show the persistence of comparable cardiac irregularities over a period of at least six years, without any appreciable cardiac difficulties even during his severe mental illness.

Case D. A man, aged 58, was seen after an attack of influenza. He felt uncomfortable when walking, but he would not admit of any dyspnœa, palpitation, or œdema. He had become liable to attacks of giddiness, and had lost consciousness on several occasions. His heart was normal in size. Systolic murmurs were audible in all arcas. His arteries were degenerate and his blood pressure was 155/110 mm. His pulse numbered about 66 per minute and was irregular—a fairly regular sino-auricular rhythm, with at times sino-auricular block, type B (Fig. 6).

After resting for a couple of months his health improved, though the sino-auricular block persisted. He returned to work, but after a year retired from business. Three years later anginous symptoms arose, and a year later he had a slight stroke. His heart was now enlarged, the mitral valve incompetent, and his blood pressure lower, 140/90 mm. His pulse was fairly regular and numbered about 66. The electrocardiogram showed a normal rhythm, but evidence of myocardial damage. He died a year later in an anginous attack.

In this patient sino-auricular block was present at a time when, although his heart was unsound, cardiac symptoms were in abeyance ; and had ceased, at a later date, when cardiac symptoms were clamant.

Case E. A well-to-do plumber came under observation in 1932, at the age of 61. He had contracted syphilis at 57. He had had a cough for many years, and was short of breath upon exertion, and liable to attacks of dyspnœa, sometimes without obvious cause. There was a chronic broncho-pneumonia at the left base. With care he regained fair health, leading a quiet life. In 1936, when he was seen after an attack of tonsillitis, merely complaining of shortness of breath upon exertion, the basal consolidation appeared to be larger than before.

In 1932 his heart seemed normal in size. The first sounds were rather weak and distant, and the second sound was doubled. His pulse numbered about 67 and was irregular ; there was a fairly regular sino-auricular rhythm, with at times sino-auricular block, type B (Fig. 9). In 1936 his heart seemed unaltered, but the doubling of the



FIG. 9.—Sino-auricular block : type B. Case E : 1932. The first beat is of sinus origin and is followed by two beats in response to auriculo-ventricular nodal stimuli, succeeded by two beats of sinus origin. Lead III.

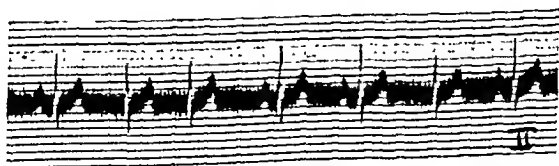


FIG. 10.—Sino-auricular block : type B. Case E : 1936. The second, third, and sixth beats are in response to auriculo-ventricular nodal stimuli. Lead II.

second sound had ceased. The pulse, 60-70 per minute, was again irregular. The electrocardiogram showed an intermittent sino-auricular block as before (Fig. 10). Both sets of records showed sinus irregularity and auriculo-ventricular nodal irregularity, the diastolic periods preceding the nodal beats being of very variable duration.

Case F. A man, aged 32, came under observation on account of breathlessness

and palpitation upon exertion. He had a well-marked mitral stenosis, of rheumatic origin. His pulse, numbering about 90 per minute, was irregular. The electrocardiogram showed slight sinus irregularity, and at times sino-auricular block, type B (Fig. 11). He remained in fair health for the next five years, save for occasional attacks of cardiac failure associated with bronchitis. He then had a hemiplegic seizure, and died shortly afterwards.

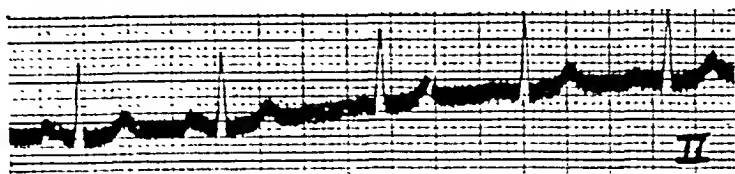


FIG. 11.—Sino-auricular block : type B. Case F. The last three beats are in response to auriculo-ventricular nodal stimuli. Lead II.

The following record is interesting as the changes in rhythm were associated with a cardiac infarct, the only instance in my experience.

Case G. A man, aged 63, had led a wandering life in his early days, been careless in his habits, and contracted many infections. For a year he had been liable to palpitation and giddiness upon exertion. A fortnight before his visit he had had a severe attack, and had been in bed for a few days.

He was a well-built man but obese. He did not look seriously ill, and a minimal amount of œdema on the shins was the only sign of cardiac insufficiency. His heart was large, and double murmurs were audible over the sternum. His blood pressure was 200/65 mm., and his arteries showed gross degenerative changes. It seemed clear that he had had an infarct. With care his health improved, and a year later he had few discomforts if he lived quietly. He had had several syncope attacks, of short duration. His heart was larger than before, his blood pressure 245/70 mm., and the albuminuria considerable. He refused to rest ; and a few months later, when in church, he had another infarct, and died two days later.

Electrocardiograms were taken on three occasions. The first (1928) showed an irregular sinus bradycardia (Fig. 12), with a pulse rate of about 30 per minute. In the upper record the rhythm is apparently normal, while the lower shows dissociation with interference, the aberrant complex of the captured beat denoting impaired conduction in the bundle branch on account of the prematurity of the contraction. The second record, a year later, shows a variable sino-auricular block, the auricular rhythm being very irregular and infrequent, and the long pauses allowing the lower centre to capture, or supplement, the ventricular rhythm (Fig. 13). The last record, a fortnight later, showed an almost regular sinus rhythm, with a pulse rate of about 40. The P-R interval measured 0.18-0.20 in. (Fig. 13). The irregular sinus bradycardia may have been due to impairment of the blood supply to the sino-auricular node. Barker and Kinsella (1924) reported a case of sino-auricular block in a dog that had an acute streptococcal infection ; the almost normal sino-auricular node was completely surrounded by an inflammatory mass.

Cutts (1937) has recorded several cases in which the pacemaker "wandered" from the sino-auricular to the auriculo-ventricular node and back again, in an irregular fashion. The cause of the change of rhythm was evidently varied. One patient, aged 37, complained of general weakness and a tremor of the head for six years. Her pulse was known to have been infrequent for many years. At the time of observation it numbered about 48 per minute, and was irregular.

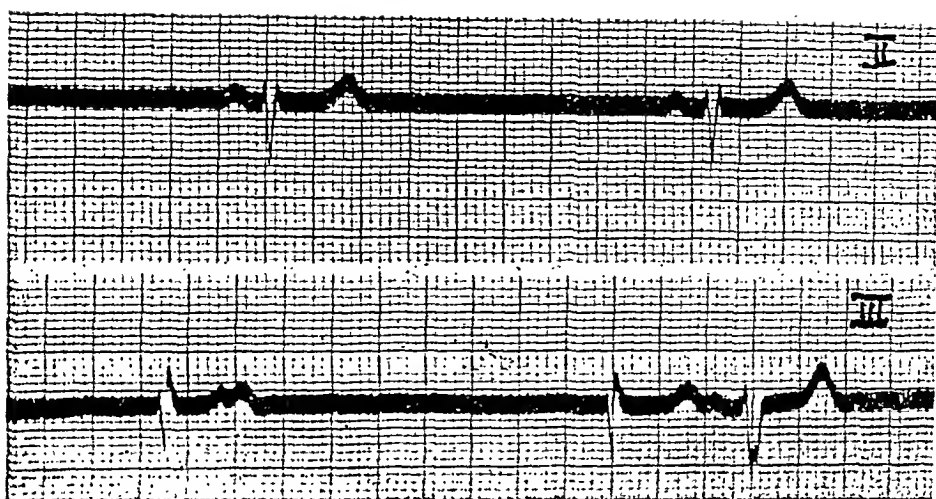


FIG. 12.—Dissociation with interference. Case G. The upper record shows an apparently normal sinus rhythm, with an abnormally slow rate, about 30 per minute. The lower record shows dissociation with capture of the third ventricular systole by the preceding auricular stimulus. The abnormal ventricular complex indicates impaired conduction in the bundle branch. Leads II and III.

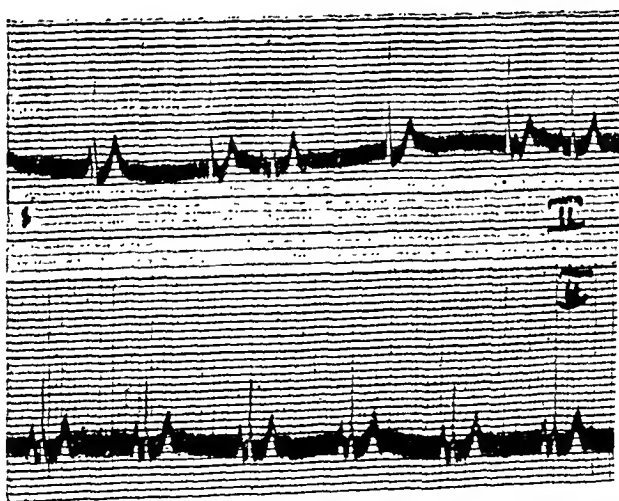


FIG. 13.—Sino-auricular block: type B. Case G. The upper record shows that the auriculo-ventricular node sets the ventricular rhythm whenever diastole is unduly prolonged. The lower record shows a return to normal sinus rhythm. Lead II.

Her heart seemed to be sound. She made a satisfactory recovery and was well six months later. There was a well-marked sinus irregularity, and when diastole was prolonged the auriculo-ventricular node took charge, and, as in some beats an inverted P was present between R and T, evidently originated these auricular contractions.

Another patient, aged 27, was suffering from rheumatic fever, and was fevered at the time of observation ; she had aortic and mitral valvular disease. The pulse numbered about 80, and was irregular. There was little difference in the rate set by the two nodes, and at times the auriculo-ventricular node took charge of the ventricular contractions. As the Ps were positive, when present, there was evidently a retrograde block. The data suggest an enhanced irritability of the auriculo-ventricular node as the cause of the altered rhythm. The patient's health improved, and she was sent home for further rest.

Some other reported cases appear to be examples of sino-auricular block, although the proof is not complete. Lewis (1925) refers to an athlete whose regular pulse of 36 when at rest abruptly rose to double that rate upon moderate exertion, and to a case reported by Neuburger and Edinger, where syncope frequently followed defæcation ; an aneurysm of the basilar artery, exerting pressure upon the medullary centres when the blood pressure rose during the act, seemed the probable cause of the attacks : and to Gerhardt's case, where similar attacks were associated with a tumour involving the left vagus nerve. Osler (1909) described a patient who suffered from attacks of syncope with an infrequent pulse of 10-12 per minute, associated with tubercular disease of the first and second cervical vertebræ. The case of de Zarday (1936) is definite ; in a woman, aged 42, suffering from a tumour in the posterior fossa of the skull, the pulse showed intermissions after each sixth systole, due to sino-auricular block. The intraspinal pressure was high, and a normal rhythm ensued for several hours after lumbar puncture. She died during an attempt at encephalography, but a post-mortem examination was not secured.

CONCLUSIONS

Sino-auricular block is not necessarily accompanied by cardiac symptoms. Four cases came under observation on account of symptoms other than cardiac ; nine cases on account of cardiac symptoms. The heart may be apparently sound (six cases) ; or may show signs of organic heart disease (seven cases).

Sino-auricular block can only be recognized by polygraphic or electrocardiographic examination. It may be suspected as the cause of recurrent syncopes in patients who show, between attacks, gross sinus irregularity.

The presence of sino-auricular block does not affect the cardiac prognosis or treatment in the individual case ; which must be based upon the general rather than the cardiac picture.

III. DISSOCIATION

Fig. 14 shows an example of dissociation with interference, from the old man (case A) reported on p. 7. His pulse then was fairly regular save for

occasional extrasystoles, the auricular rate 32·7 per minute, and the ventricular rate 32·8. At first the P precede waves QRS with a narrowing interval. Later

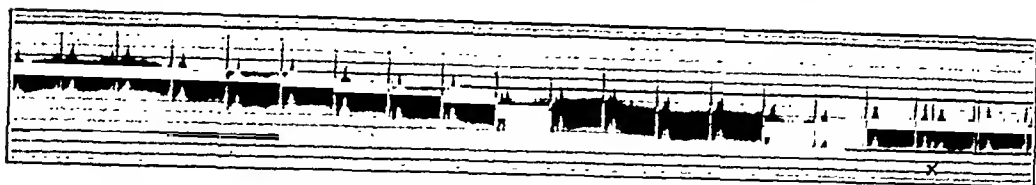


FIG. 14.—Dissociation with interference. Case A. See text. The ventricular beat 18 (x) is due to capture by the preceding auricular stimulus. Lead I.

they become lost in R and then emerge between R and T. Finally P fuses with T and again becomes invisible. As this auricular stimulus reached the ventricle at a time when it was excitable, it was followed by a ventricular contraction (x) : (capture). With care his pulse rate rose to normal figures, and 3 months later numbered 66 and was almost regular, P preceding QRS by about 0·20 in. On this occasion sino-auricular block was recorded (Fig. 2) ; it continued until his death a month later.

Case H. This patient has been under observation, at intervals, for many years. He was born in 1865. A well-built, muscular man, he engaged in athletic pursuits in early life, but permitted himself to become stout and flabby at an early age. He has had many adventures ; infections of varied character ; and has consistently "done himself well." In 1895 G. A. Gibson sent him to bed for cardiac symptoms, accompanied by œdema, which had followed athletic feats on the hill. In 1912 he became subject to attacks of giddiness, probably related to chronic otitic media, and had become unable to sustain continued exertion. "A lion before lunch ; a mouse after it." He made similar complaints in 1916 and 1921, and became very nervous. In 1925 he had two syncope, following long drinks after shooting all day. He was now short of breath upon exertion. In 1930 he had to cease shooting as he tired easily. In 1936 he was leading a quiet life, and was very well.

His heart has always been normal in size, and his blood pressure has never been high ; his arteries are soft. In 1926 QRS was splintered and T3 inverted, but the Ts were positive after 1928. His pulse has been slow—51–57–64—and often irregular from extrasystoles ; in 1926 it showed functional dissociation without interference (Fig. 15). A similar irregularity was noted in 1930, but the rhythm was normal in 1912, 1916, 1921, and 1928.

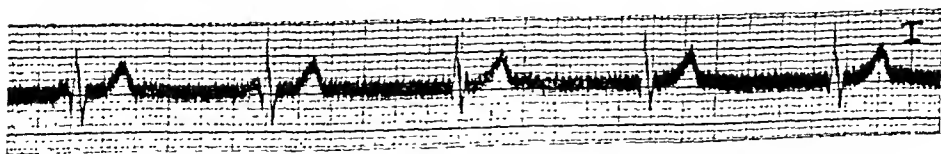


FIG. 15.—Dissociation. Case H. The P-R intervals of the first two beats are shortening, and the succeeding Ps are lost in QRS. Lead I.

Case I. This patient came under observation at the age of 53, on account of pain in an elbow following trauma. He suffered from chronic bronchitis and was liable to asthma. His heart seemed normal to physical examination, but the pulse was slightly irregular and an electrocardiogram showed well marked R-T deviation in leads II and III, and also slight sinus arrhythmia and auriculo-ventricular dissocia-

tion (Fig. 16). Three days later the sinus irregularity still persisted, but the rhythm was normal and the R-T deviation was less marked. Nine years later he is in fair health and at work. He has never shown any symptoms suggestive of cardiac insufficiency.

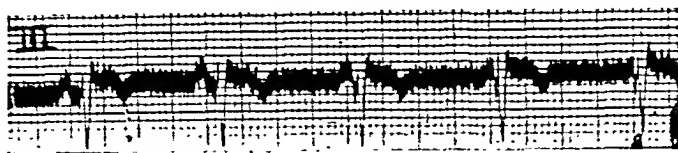


FIG. 16.—Dissociation. Case I. The P-R intervals of the first three beats are steadily shortening. The fourth P merges into R, and the fifth is lost in the ventricular complex. Lead III.

Another example of auriculo-ventricular dissociation was shown in Fig. 12, obtained from case G. White (1916) reported the case of a woman, aged 24, whose heart appeared to be sound. When convalescing after removal of the tonsils four days previously, her pulse was noticed to be slightly irregular and she complained of palpitation. The electrocardiogram showed dissociation, the auricles beating 67–85 times per minute and the ventricles 96. Next day the rhythm was normal, but dissociation was readily produced by pressure upon either carotid sinus, which slowed the auricular rate from 80 to 68, and thus permitted the escape of the auriculo-ventricular node. She was up and about at the time of the observation.

Hewlett (1923) reported the case of a man, aged 75, seen for shortness of breath, œdema of the feet, and pain in the chest upon exertion. His heart was enlarged, with a diastolic murmur sometimes audible at the apex, and a raised blood pressure, 175/110 mm. At intervals over a period of months dissociation was present; generally the ventricular contractions (84, 88, 84, 75) were more frequent than the auricular (73, 71, 71, 72), but on one occasion the auricular rate was 75 and the ventricular rate 66. The pulse rate varied between 66 and 96. Atropine increased the ventricular rate and pressure over the carotid sinus slowed it. Large doses of digitalis slowed the auricular rate, but did not affect that of the ventricles.

Enescu and Vacareanu (1934) reported two cases of dissociation. One was suffering from rheumatic fever; some sinus arrhythmia was present, with a pulse rate of 56. On the fourth day dissociation was recorded, there being but little difference between the auricular and the ventricular rates. The rhythm had returned to normal three days later. The second man, aged 32, complained of attacks of vertigo, and his pulse numbered about 68. There was usually sinus arrhythmia, and a P-R interval of 0.22 in. On one occasion dissociation was present, with a pulse rate of 61. The general picture suggested myocardial mischief. Neither of these patients had taken any digitalis.

Ritchie (1935) reported two cases of dissociation. One, a woman aged 44, was admitted into hospital on account of congestive failure, due to a diffuse myocardial fibrosis. After some improvement, the pulse rate falling from 90 to 60–63, she soon relapsed and digitalis was exhibited. The rhythm was

normal, but five days later interference dissociation was present, the auricular rate being 60.7 and the ventricular rate 73.1 per minute. She died two days later. His second case, also a woman aged 44, was suffering from congestive failure, with mitral stenosis. She had been taking digitalis for some months prior to admission. Dissociation was present, the auricular rates being 42, 45, 57 and the ventricular rates 75, 74, 87. It continued until her death eleven days later.

CONCLUSIONS

The conditions which were associated with the occurrence of dissociation in these ten cases were varied. In one it accompanied an infarct; and in seven cases there was evidence of myocardial mischief. In two the heart was apparently sound. Dissociation is often associated with the administration of digitalis, and accompanied it in several of the cases mentioned above; but in four cases no digitalis had been given.

There are no special symptoms associated with dissociation. In four of these patients symptoms of cardiac insufficiency were present, and two complained of cerebral symptoms. One was suffering from rheumatic fever, two merely complained of irregularity of the heart, and one made no complaint referable to the heart.

Dissociation can only be recognized by electrocardiograms. Its occurrence does not affect the outlook from the cardiac standpoint. It does not call for any specific treatment, but its frequent association with the administration of digitalis suggests that the dose, if not altogether discontinued, should be of moderate amount.

IV. THE NODAL RHYTHMS

The various forms of auriculo-ventricular nodal rhythm may be conveniently divided into three clinical groups:

- (1) those with paroxysms of tachycardia;
- (2) those with a persistent frequent pulse rate;
- (3) those with the pulse rate unaltered, or less frequent than normal.

(1) *Paroxysmal Nodal Tachycardia*.—This group is the most common form of paroxysmal tachycardia (146 of 325 cases). It occurs at all ages, and need not occasion any distress save palpitation, unless, from long continuance of the tachycardia or pre-existing cardiac disease, the muscle of the heart becomes exhausted. The clinical story is varied.

Case J. A healthy boy of 16 had had attacks of palpitation at irregular intervals as long as he could remember. They lasted for variable periods, sometimes for several days. During the attacks the pulse ran about 220–240 per minute. Between attacks he was fit and well. His organs seemed sound.

Case K. An active country gentleman found, at the age of 69, that he was becoming subject to attacks of palpitation and shortness of breath upon exertion, steadily increasing in frequency and severity. During the attacks the pulse numbered about 136 per minute. His blood pressure, heart, and blood vessels seemed in reason-

able condition for his age. The electrocardiogram showed that P was hidden in R. After a few months hepatic colic ensued, and a gall-stone was removed successfully. The attacks then lessened in severity, and he became able to resume his former field activities. Ten years later he is leading a quiet life and in reasonable health. The attacks are now infrequent and of short duration.

If, however, the heart is already weak the outlook is serious.

Case L. A done old man, aged 77, was admitted into hospital complaining of attacks of giddiness, and of faints in some of which he had fallen to the ground. He was emaciated, childish, and restless, and steadily deteriorated both mentally and physically during his residence.

Many attacks were witnessed. The striking feature was failure of the pulse. If the failure was of short duration, a few seconds, he became restless and sometimes ceased to breathe; if for 10 seconds he became very pale and lost consciousness. On several occasions when the pulse failed for a longer period the muscles twitched, and less often generalized convulsions ensued.

His heart was normal in size and site. The sounds were closed but short and distant. All his arteries were tortuous and thickened. His blood pressure varied: 115-155/60-95 mm. The cardiac rhythm was very unstable. His pulse might be regular even for days, but was often irregular from extrasystoles, which might be isolated events in a long series of regular beats, or, more often, bigeminal, trigeminal, or wholly irregular in incidence. When the radial pulse failed the cervical veins at once became greatly distended, pulsating vigorously at about double their usual rate (160 per minute). Polygraph tracings showed large venous waves and lessened arterial volume (Fig. 4). The electrocardiogram showed an inverted P between R and T. It was clear that the tachycardia rapidly exhausted an already weakened myocardium.

In several of our patients, with a degenerate heart, attacks of paroxysmal tachycardia were associated with serious symptoms if the attack lasted for long, or as age increased.

Case M. A man who was recognized to have paroxysmal nodal tachycardia at the age of 60, had probably had his first attack at the age of 27, following typhoid fever. The attacks ceased for some years, but recurred at the age of 50, and continued. He had a high blood pressure and degenerate arteries. In his early life the paroxysms occasioned little discomfort, but as he grew older caused great exhaustion. He aged quickly, the attacks recurred every month, and when 63 an attack occurred and persisted, the pulse running 180-200 per minute until death ensued after 72 hours.

(2) *Continued Nodal Tachycardia.*—In a small number of cases nodal tachycardia has been observed in patients suffering from an infective disease, most commonly acute rheumatism and "bacterial" endocarditis. The onset of the rhythm may be preceded by nodal extrasystoles.

Case N. A man, aged 27, was admitted into hospital in 1922, suffering from acute rheumatism. Both the mitral and the aortic valves were affected, but he made a good recovery and resumed his work. In 1925 symptoms of cardiac failure ensued, followed by arthritis, and his progress was unsatisfactory; the congestive symptoms increased, many veins became thrombosed, and infarcts occurred in the lungs and spleen. He died in February 1926, evidently with a "bacterial" endocarditis. During his last illness his fever was never high, not exceeding 101° F. His pulse at first was regular, numbering about 100 per minute. But five days before his death it rose to 150-160, and continued so until the end. The electrocardiogram showed a nodal rhythm, an inverted P appearing between S and T (Fig. 17).

Case O. A man, aged 42, was admitted into hospital on the fifth day of an acute pneumonia. His pulse was frequent and regular save when interrupted by an extrasystole. Next day there was a regular nodal rhythm, with a hidden P at the rate of 144 (Fig. 18). Next day his auricles were fluttering, and continued to flutter until

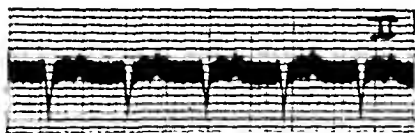


FIG. 17.—Nodal rhythm. Group 2. Case N. An inverted P is visible between S and T. Lead II.

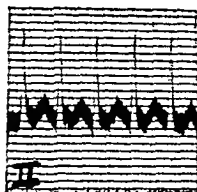


FIG. 18.—Nodal rhythm. Group 2. Case O. P is lost in the ventricular complexes. Lead II.

his death on the ninth day of illness. The mitral and aortic valves showed chronic endocarditis, with superadded acute re-infections. The myocardium showed an extensive patchy fibrosis. The nodes, unfortunately, were lost.

Cowan *et alii* (1913) reported six cases of acute endocarditis whose polygraph tracings showed a short *a.c.* interval. Microscopic examination disclosed involvement of the *a.v.* nodes in acute inflammatory lesions. The cardiac rhythm in these patients was regular, save for occasional extrasystoles, the maximum rate in the several cases being 105, 120, 140, 140, 140, 145 per minute.

Hume (1914) reported the occurrence of nodal rhythm during a small epidemic of diphtheria. A girl, aged 7, showed auricular extrasystoles on the ninth day of illness; nodal rhythm with a pulse rate of 109 on the tenth and eleventh days; auricular flutter on the twelfth day; and a regular rhythm save for some auricular extrasystoles on the thirteenth day. She died on the fifteenth day of illness. A gross interstitial myocarditis was found, the *a.v.* node and bundle being unaffected. A boy, aged 7, had a normal rhythm on the seventh and eighth days of illness; extrasystoles on the ninth day; nodal rhythm with a pulse rate of 94 on the tenth day; and 2-1 heart-block on the twelfth and thirteenth days. He died next day. The *s.a.* node was acutely inflamed and the *a.v.* bundle was engorged. The *a.v.* node, unfortunately, was lost.

(3) *Nodal Rhythm without Tachycardia.*—In this group the pulse rate is little altered, or less frequent than normal.

Case P. A gamekeeper, aged 55, was seen in 1914 for a strain of his right shoulder which had kept him off work for some weeks. He was a sparely built fellow, who looked younger than his years. He would not admit of any disability, and said that he could carry 14 couples of rabbits for a mile and a half without discomfort. His brachial arteries were thick and tortuous, but his heart seemed sound. His pulse numbered 75. The electrocardiogram showed normal ventricular complexes, and an inverted P, less than 0.10 sec. in front of R (Fig. 19). A fortnight later the rhythm was unaltered. He continued at work, but refrained from carrying heavy weights. A year later he was in good health. On this occasion the cardiac pacemaker was mobile, wandering between the sino-auricular and the auriculo-ventricular nodes,

though the pulse rate (69) did not alter. A normal rhythm, with P-R 0.14 in., changed within a couple of beats to a nodal rhythm with an inverted P, less than 0.10 in. before R (Fig. 20). The normal rhythm returned shortly afterwards, but the

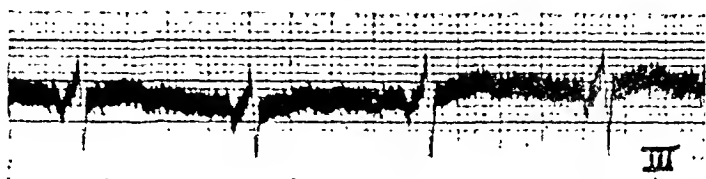


FIG. 19.—Nodal rhythm. Group 3. Case P. P is inverted and precedes RS by 0.08–0.10 sec. Lead III.



FIG. 20.—Nodal rhythm. Group 3. Case P. This record shows the transition from the sino-auricular to the auriculo-ventricular rhythm. Lead II.

change was not observed. In 1919, 1920, 1921 he was in good health, with a normal rhythm. In 1936, at the age of 76, he is still active as a griever, and looks well and young for his age. His organs seem healthy and the cardiac rhythm is of sinus origin. An occasional extrasystole was missed in the electrocardiogram.

Boukspan (1928) reported the case of a locksmith, aged 29, who showed a nodal rhythm, with a pulse rate of 36–40, over a period of seven months. He had suffered from syphilis five years before, but the Wassermann test was negative. The first sound at the apex was “rough.” On exertion his pulse rate rose to 44–46, and after atropine to 75. During the period of infrequent rate P was hidden, but when under the influence of atropine it reappeared, as a positive deflexion, before or after R. He continued at his work.

Wedd and Wilson (1930) reported the case of a man, aged 22, who had an apparently constant nodal rhythm. He had had a hemiplegic stroke at the age of 16, and was weak-minded. The mitral valve was stenosed. The usual pulse rate was about 60, but at times it fell as low as 36, and it sometimes failed for several seconds. This might occur spontaneously, or be induced by scolding or a sudden order. The pace-maker was not affected by atropine, or pressure upon the carotid sinus or the eyeballs, but the rate, when infrequent, was accelerated by exercise and atropine; so the standstills were evidently vagal in origin.

Ledoux (1935) reported the case of a young farmer, aged 26, whose electrocardiograms invariably showed nodal rhythm, P appearing between R and T, over a period of eighteen months. His pulse rate was habitually infrequent,

30–60 per minute, and very variable. Syncopal attacks had recurred frequently when his pulse rate was low, but none was observed during his residence in hospital.

The following cases of nodal rhythm were under observation, at the time when the disordered rhythm was observed, on account of some form of cardiac disability.

Ritchie (1914) reported the case of a man, aged 72, with congestive cardiac failure, and high blood pressure. His pulse at first was grossly irregular with numerous nodal extrasystoles. On several occasions nodal rhythm supervened for an indefinite period, the pulse running in the nineties. Under treatment he improved, and the rhythm became normal. Another man, aged 47, was suffering from subacute myocarditis, without valvular lesions. For about a month a normal rhythm, with a pulse rate of about 90, alternated with a nodal rhythm, with a pulse rate of about 80. He improved for a time and resumed his work, but the improvement was transitory. His auricles went into fibrillation, and cardiac failure ensued. He died three and a half months after coming under observation. The cardiac muscle showed widespread fibrosis and cellular infiltration. The a.v. node and bundle were grossly involved.

White (1915) reported the case of a man, aged 37, who complained of obesity and weakness of the legs, probably due to early tabes dorsalis. His heart was normal in size and the sounds were closed and of fair value. His pulse on admission was 120, and there was a uricular flutter with defective conduction in the bundle branch (Type I). Ten days later the auricles were fibrillating. Four days later the rhythm was nodal, and this persisted for the next four months, the pulse rate falling to 40–43.

Matthewson (1915) reported the case of a man, aged 22, whose pacemaker frequently changed from the sino-auricular to the auriculo-ventricular node. He complained of shortness of breath and palpitation. His mitral valve was incompetent. His pulse numbered about 70 and the change of pacemaker recurred without any obvious change in the rate of the pulse, either node becoming dominant in an inconsistent fashion. When the rhythm was nodal compression of the carotid sinus failed to influence the pacemaker, but atropine and gentle exertion caused a return to normal rhythm.

A woman, aged 62, reported by Fussell and Wolferth (1920), had complained of attacks of palpitation since childhood, at first of little moment, but gradually increasing in frequency and in severity, till she had been forced to lead an invalid life for a couple of years. She had become short of breath upon exertion, and had noticed some œdema of the feet. After leaving hospital she died from cardiac failure. Her heart was slightly enlarged, and the mitral valve was incompetent. The attacks of palpitation occurred at any time, on exertion or during sleep. They could always be checked by holding her breath. They were due to an auricular tachycardia, and the pulse rate rose to 135 per minute. Her pulse rate was very variable, as the pacemaker shifted irregularly between the sino-auricular and the auriculo-ventricular nodes, the nodal rhythm persisting for a few seconds or as long as several minutes. The nodal rhythm might develop gradually, with decreasing P–R intervals, the rate gradually

slowing to 30–45 per minute ; or suddenly without any appreciable change in rate.

Richardson (1922) reported the case of a woman, aged 47, who was suffering from mitral disease and chronic nephritis. A normal rhythm, with a blood pressure of 150/98 mm., changed under the influence of digitalis to a nodal rhythm, with a pulse rate of 38–43 and a blood pressure of 180/120 mm. Atropine and pressure over the carotid sinus had no effect upon the pacemaker. She died eventually from pneumonia. The mitral and tricuspid valves were thickened, and the aortic valve acutely inflamed. Scars were present in the right auricle, and the ventricles showed a general fibrosis. The *s.a.* and the *a.v.* nodes were normal.

CONCLUSIONS

Causation of the Nodal Rhythms

1. *Paroxysmal Nodal Tachycardia*.—The nature of the paroxysmal change in rate is not clear. The sudden onset and termination of the paroxysms suggest a nervous cause, cessation of the controlling activity of the vagus, or overaction of the accelerator mechanism. But the failure of vagal stimulation to control the tachycardia, save in very exceptional cases, shows that the nervous control is temporarily lost, from some obscure cause.

2. *Continued Nodal Tachycardia*.—Continued nodal tachycardia has hitherto been observed only in cases of acute myocarditis, and the change in rhythm is presumably due to involvement of the auriculo-ventricular node in an inflammatory mass.

3. *Nodal Rhythm without Tachycardia*.—This group in which the pulse rate is unaltered or slowed evidently owns several causes. In some patients the heart is apparently sound, in others grossly diseased. In some the change of rhythm ensues during the exhibition of digitalis and ceases on withdrawal of the drug. In some the normal rhythm follows the administration of atropine, but in others the abnormal rhythm is unaffected. It thus seems clear that some cases are due to vagal overaction, whether spontaneous or induced by digitalis, and the consequent domination of the rhythm by the auriculo-ventricular node. But the cases which are not influenced by atropine must own a different cause, perhaps of myocardial origin.

Diagnosis of Nodal Rhythm

This can only be established by polygraphic or electrocardiographic records. Its occurrence can sometimes be suspected by the appearance of large pulsatile waves in the jugular veins, caused by the coincident contraction of the auricles and ventricles, closing the tricuspid valve and so entailing the reflux of the auricular blood into the veins when the right auricle contracts.

Prognosis of the Nodal Rhythms

1. *Paroxysmal nodal tachycardia* is not incompatible with long life. In patients whose hearts are sound, and cardiac reserve between paroxysms ample, the immediate and the ultimate outlook is good. If an attack persists for many hours symptoms of cardiac insufficiency may arise, but they rapidly subside on cessation of the tachycardia.

The outlook is, however, serious in patients whose hearts are unsound, as the tachycardia rapidly exhausts an already weakened heart; and is more serious if symptoms of cardiac weakness already exist.

2. *Continued nodal tachycardia* always makes the outlook serious, as it seems to be indicative of acute myocarditis. Its occurrence in the cases hitherto reported has always been followed shortly by death.

3. *Nodal rhythm without tachycardia* with an unaltered or a slowed pulse rate has a variable outlook according to the cause. It is serious in the cases where the alteration in rhythm is due to a myocardial lesion and in those due to digitalis, as the exhibition of the drug predicates some pre-existing cardiac difficulty. In the nervous cases the outlook is good.

V. SUMMARY

Alterations in the rhythm of the heart, as isolated signs, are not necessarily of serious significance.

James Mackenzie stated (1912) that *sinus irregularity*, in a healthy individual, was a normal occurrence, and many observers have subsequently confirmed the accuracy of his dictum. It is true that *sino-auricular block* may, as shown in some of the cases which we have collected, be accompanied by serious symptoms, but the subsequent history of these patients shows that, in the absence of signs of cardiac disease, the prognosis from the cardiac standpoint is quite good. Any danger lies in the nature of the nervous disorder which occasions it.

The occurrence of *extrasystoles*, *per se*, has not any sinister significance. It is true that if they recur rapidly for long periods the mere rapidity of the cardiac contractions may produce cardiac failure, but, in the absence of signs of cardiac disease, any cardiac symptoms rapidly pass as soon as the normal rhythm is restored. A man, who died from paralysis agitans at the age of 75, had been liable to attacks of paroxysmal tachycardia from the age of 18, and had lived a very strenuous life for many years.

The prognosis in cases of *nodal rhythm* depends, as in *sinus irregularity*, upon the nature of its cause. The outlook is serious if it is due to myocardial lesions; but good if it is due to nervous causes.

The occurrence of *auricular fibrillation* is generally a signal of impending danger, but the exceptions to the rule are fairly numerous. Cases have been reported where the arrhythmia persisted for ten or even twenty years. One of my patients bore a child safely although her auricles had been in fibrillation for at least three years. The irregularity is not the important factor in the

failure. The danger lies in the frequency of the ventricular contractions or in the continued activity of the cause of the irregularity. Fibrillation may be due to several causes : pathological lesions in the auricular muscle, of chronic or acute character ; auto-intoxications, as in Graves' disease ; poisons introduced from without (digitalis, anæsthetics, coal-gas poisoning, etc.) ; physical stresses ; and perhaps to disturbances of the nervous control of the heart (Cowan 1929). The cause may be permanently or temporarily in action. The prognosis follows the cause.

Heart-block and bundle branch block repeat the story. As they are most frequently due to myocardial disease the prognosis is, as a rule, serious, but many patients live in fair health for many years. Again the danger lies in the rate of the ventricular contractions, or in the character of the process which has disturbed the rhythm of the heart.

This paper is based upon electrocardiographic records, upon what may be called laboratory methods of diagnosis. But it seems to me that there is a tendency at the present time to overestimate the value to clinical medicine of such methods. The wood tends to be hidden by the trees, and an attempt is made to treat a symptom, or even a sign, and not a sick man.

An irregular pulse is a useful signpost, but the causes of irregularity are numerous, and not necessarily disease of the heart. In many cases treatment, if it is to be helpful, must be based upon the general picture of the illness, and directed to regions outwith the heart.

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DIGITALIS IN HEART FAILURE WITH NORMAL RHYTHM

BY

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In the first edition of his *Diseases of the Heart*, published in 1908, Mackenzie said : " the nodal rhythm is present in the majority of cases of severe heart failure and in a great many the immediate breakdown is directly attributable to the inception by the heart of this abnormal rhythm." In the third edition, in 1913, the term " auricular fibrillation " was substituted for that of " nodal rhythm," the researches of Lewis and others having established their identity. Mackenzie gave the proportion as " 60 or 70 per cent. of all cases of serious heart failure met with in practice." It is even now generally admitted that auricular fibrillation affects the majority. Lewis (1937) has said that at least 70 per cent. of all cases of failure with congestion display fibrillation.

To quote Mackenzie (1911) on digitalis : " Cases of auricular fibrillation are more readily and more markedly affected than cases with normal rhythm." Dissident views began to be expressed perhaps first by Janeway (1913), and later especially by Christian (1919) whose paper was entitled " Digitalis therapy : satisfactory effects in cardiac cases with regular rhythm." In a further study (Christian, 1922) he affirmed that : " Digitalis is fully as effective in the treatment of chronic cardiac cases without auricular fibrillation as it is in those with fibrillation." Luten (1924) reached the same conclusion. Yet most authors to-day admit that the beneficial effect is greater in auricular fibrillation, though they do not deny (and Mackenzie did not) that it is also effective in heart failure without fibrillation. Lewis's experience is that occasional cases presenting regular heart action respond favourably (Lewis, 1937).

We have spoken as if auricular fibrillation occurred indiscriminately in heart failure and as if the response to digitalis depended simply on the presence or absence of this arrhythmia. But it might be that fibrillation connoted a different group of cardiac lesions and thereby a different reaction to digitalis. It was with this idea in mind that Parkinson and Clark-Kennedy (1926) undertook an inquiry into heart failure with normal rhythm. It was established that there is an important relation between the pathological basis for a cardiac disease and failure and the presence or absence of fibrillation. In general,

auricular fibrillation was the rule in rheumatic heart disease and goitre, while failure with normal rhythm was the rule in hypertension, coronary disease, and emphysema.

Apart from the factor of rhythm and the factor of a specific pathology conditioning rhythm, there is a third factor of the *heart-rate* during failure. A regular rhythm failure may occur with a normal or moderate ventricular rate, or a high rate. This has been much discussed (Mackenzie, 1911 ; Sutherland, 1919 ; Christian, 1922 ; Hay, Jones, and Ince, 1927 ; Marvin, 1927 ; and Luten, 1936 *a, b*). Apart from its pharmacological interest, the rate in failure with normal rhythm might indicate where *digitalis* acts beneficially, e.g. those with a high rate might respond and those with a normal rate might not respond.

The question we have placed foremost in this inquiry is how often and how far *digitalis* can help in a clinical sense patients who are suffering from heart failure without auricular fibrillation. It was hoped also to learn something from the kind of failure, the ætiology, the pathological basis, or the ventricular rate, which would aid in selecting the patient most suited for *digitalis* treatment. This clinical discrimination in the use of *digitalis* in heart failure with normal rhythm should soon be settled, because a mercurial diuretic will in future so often be employed alone or along with it that the separate effect of each should be established.

METHOD OF INVESTIGATION

Our observations were made chiefly on patients admitted to the beds of the Cardiac Department of the London Hospital over a period of eighteen months ending July 1938. Every patient considered to be suffering from congestive heart failure with normal rhythm was admitted for therapeutic observation. A combination of two or more of the following criteria was required : obvious dyspnœa, œdema, enlargement of the liver, congested lungs with or without hydrothorax, and venous distension in the neck. Left ventricular failure with paroxysmal dyspnœa and without systemic congestion was excluded from this inquiry. The degree of failure was assessed as slight or as moderate to severe. An electrocardiogram was taken. The chest was examined by X-rays and by teleradiograph when necessary. If a hydrothorax was present, teleradiograms were taken at intervals to register progress. The Wassermann reaction was tested except in a few of the rheumatic group. The blood urea was estimated and primary renal disease was excluded clinically and occasionally by necropsy.

For a period of at least a week no active treatment was ordered and the patient simply remained in bed. If *digitalis* had been given before admission, this control period was extended. A few patients were so ill on admission that strophanthin or salyrgan had to be given intravenously ; if so, an additional period without drugs was arranged. But if at about the fifth day of rest alone a patient was worse, it was felt unnecessary to withhold *digitalis* any longer for control purposes. A sedative (usually morphine) was given at night if required. Fluids were not often restricted and so the disturbing factor of another therapeutic measure was avoided. It proved that 40 oz. (1,137 c.c.) daily was

seldom exceeded, but in a few where fluid was restricted to 30 oz. (852 c.c.) the restriction was equally applied during the rest and the digitalis period. Frequent clinical notes were made in order to assess the rate and the extent of any improvement in the symptoms and signs of failure. During the control period we had to reject a number of cases because of pyrexia or other complications such as pulmonary infarction. Sometimes rest in bed alone was so beneficial that the residual failure was incompatible with adequate observations on digitalis action.

The Digitalis Course

Digitalis was administered in friable tablets containing one grain of the powdered leaf, *pulvis digitalis folia*, B.P., which is standardized biologically to contain 10 international units per gramme. This preparation is identical with that in the United States Pharmacopœia of 1936. The usual dose was 2 grains three times a day (6 grains or 0.4 g. daily). In the early cases 1 grain three times a day was given for 14 days, but its effect was less easily demonstrated. Sometimes 3 grains three times a day were given and then usually in the more resistant cases or at a subsequent test. The normal period of digitalis administration was 7 days. It was found that 2 grains three times a day was a practicable dose and rarely led even to slight toxic effects, and then only towards the end of the test.

Certain criteria were considered for determining the result of rest in bed alone and of the digitalis course. Little attention was given to the patient's feelings expressed in response to the usual polite enquiries, for these are so much influenced by the patient's good will. Observed dyspnœa at rest or on slight movement was important, as were also the degree of distress and obvious discomfort including cough, insomnia, epigastric (hepatic) discomfort, and flatulence bound-up with failure. The rate of the respiration was charted, but it seemed little related to the degree of dyspnœa as felt by the patient or observed by the physician. As Christian (1922) said: "Dyspnœa is poorly, sometimes not at all, depicted by the charted rate of respiration." Crepitations at the bases of the lungs were not of much value, as they often disappeared with the first few days of rest. Hydrothorax always figured in the rating, but its place and importance would scarcely have been realized had X-ray examination of the chest in failure not been practised. So objective a sign as œdema must always be an important index of progress. The size of the liver was almost as important. Diuresis and loss of weight were valuable criteria. The venous distension did not prove generally serviceable as a guide to the progress of improvement, and the same may be said of cyanosis.

Digitalis Effect or Digitalis Benefit.—The result of the digitalis course might be considered either as a pharmacological effect or as therapeutic benefit. Fall in heart-rate was not here regarded as an indication of therapeutic benefit, and this policy enabled us to observe the relation of slowing to benefit as assessed by our criteria of improvement, e.g. loss of œdema.

In most patients only one course of digitalis was studied; but in a few cases of persistent failure two courses of digitalis were observed during the stay in

hospital. When further observations were made during a subsequent admission, the patient was regarded as a new case.

Failure with Auricular Fibrillation.—Although this paper mainly concerns failure with normal rhythm, we have also studied in like manner thirty cases of failure with auricular fibrillation for comparison. The ventricular rate was counted at the apex daily throughout both the control period and the digitalis period.

Salyrgan.—In several cases salyrgan, 2 c.c., was given intravenously either immediately following the end of the digitalis course or else a few days later, so as to judge whether a diuresis was possible by means other than digitalis. Neither ammonium chloride nor ammonium nitrate was used as an adjuvant.

Classification of Cases

The choice of cases was made primarily on the presence of cardiac failure with normal rhythm, and without regard to the ætiology of the causal heart disease. Hypertensive, rheumatic, and syphilitic heart disease together formed the bulk of the cases (Group 1-4 ; Table I). Of the ten syphilitic cases, all had aortic incompetence. Group 5 included atheromatous aortic incompetence and coronary disease without hypertension or cardiac infarction. No typical example of heart failure from emphysema was found.

There were 22 observations on 18 patients with heart failure and normal rhythm who are classified among subsidiary groups, namely: congenital heart disease, acute rheumatic carditis with valvular disease, infective endocarditis, complete heart-block, and chronic nephritis. They were treated just the same, but they were patients in whom digitalis would not usually be employed or in whom its action would be less promising. Thyrotoxic heart disease was excluded.

PREVIOUS OBSERVATIONS

The main question is how far digitalis can benefit patients with failure in normal rhythm ; and the further question is the comparable benefit in failure with auricular fibrillation. Though there are a large number of statements based only on personal experience and conviction, there are a limited number of detailed studies of these questions. The largest series are those of Christian (1922), Luten (1924), and Marvin (1927).

Christian contrasted 40 cases of normal rhythm with 57 cases of auricular fibrillation. Though without preliminary control periods, there is good evidence of successful treatment which was independent of rhythm. In both classes, his high percentage of successes is augmented by the inclusion of a reduced heart-rate as an indication of success. Possibly, too, the restricted fluid favoured his results.

Luten studied 20 cases of failure with normal rhythm. After control observation, he gave digitalis in massive doses (Eggleston method) and found that "digitalis affected most of the cases favourably." These results applied to failure from chronic myocarditis with or without hypertension or œdema.

No cases with auricular fibrillation were used for comparison, but the conclusion was that "patients with myocardial insufficiency improve under proper digitalis administration in about the same proportion of cases as do patients with auricular fibrillation."

Marvin investigated 20 cases of advanced congestive failure with much œdema, paying particular attention to ætiology in relation to the digitalis response. Eggleston's method of administration was used after a control period of observation. Benefit from digitalis followed in 11 of the 20 cases; none in the rheumatic group of 5; 3 in the syphilitic group of 5; and 8 in the arteriosclerotic group of 10; but only two cases (both in the last group) showed great improvement comparable with that seen in auricular fibrillation. Slowing occurred once only in each group.

Mackenzie (1911) was not impressed with digitalis effect in failure with normal rhythm, though he recognized that digitalis might on occasion produce a satisfactory diuretic response and independently of the heart-rate. He laid great stress on the beneficial effect of rest in bed when the rhythm was normal, and attributed to it much of the apparent digitalis response.

Hay, Jones, and Ince (1927) gave digitalis tincture until toxic symptoms appeared in nine controlled cases of failure with normal rhythm. Four cases showed benefit, the greatest being seen in rheumatic valvular disease with œdema. They found that fall in heart-rate was not necessarily accompanied by subjective improvement. Kellum (1932) studied digitalis diuresis in twelve controlled patients with failure and œdema, with one exception normal rhythm being present. Diuresis was moderate in three and slight in four cases, but fluids were restricted to an average of 770 c.c. (27 oz.) per day. The pulse was reduced in one-half the cases to an extent of an average of thirteen beats per minute. In an analysis of case records of failure with sinus mechanism, Hyman and Fenichel (1932) found that moderate doses of digitalis improved only 4 of 13 arteriosclerotic patients and none of 9 in the rheumatic group. Reduction in heart-rate itself was reckoned as evidence of improvement. In the presence of auricular fibrillation, digitalis helped 22 of 27 arteriosclerotic and all 30 rheumatic cases. Nineteen ambulatory patients with paroxysmal dyspnœa and normal rhythm were studied by Harrison, Calhoun, and Turley (1931). Sixteen cases were completely relieved by digitalis. As paroxysmal dyspnœa is a special product of left ventricular failure, we regard this result as of great practical importance. While investigating the effect of digitalis in over 100 cases of pulsus alternans in sinus rhythm, Windle (1917) opined that it could be given "with the confidence in a first attack of dropsy that it will almost surely do good." In an earlier paper dealing with rheumatic heart disease, Windle (1913) concluded that "digitalis often acts as well, as certainly, and as speedily on the general symptoms of heart disease with dropsy and regular pulse as it does in like cases of auricular fibrillation." In children under 14 with rheumatic infection and failure with normal rhythm, Sutherland (1919) concluded that the digitalis in rapid heart action was as specific in reducing the heart rate as in auricular fibrillation and that the beneficial effects were as striking. When the pulse-rate rose it could be repeatedly lowered by digitalis.

The general conclusion of these investigators is that digitalis is indicated in heart failure with normal rhythm and that it often succeeds, though not so often and seldom so well as in heart failure with auricular fibrillation. Christian (1922) and Luten (1924) are exceptional in claiming that it succeeds as frequently and as well in normal rhythm as in auricular fibrillation. Opinions expressed by West and Pratt (1920), Robinson (1923), Fraser (1924), Robinson, White, Eggleston, and Hatcher (1924), Cushny (1925), Levy and Mackie (1927), Bramwell (1937), and East (1937) support the general conclusion, which is also the teaching found in current books on cardiology, e.g. Lewis (1937), White (1937), Fishberg (1937), East and Bain (1936), Levine (1936), Cowan and Ritchie (1935), and Harrison (1935).

In French reports the rhythm is not much considered in this relation, and Laubry (1938) says that digitalis is suitable for all cases of cardiac failure. Among German books, Scherf (1938) says that quite good digitalis action can be observed in hearts in failure without fibrillation because of the drug's action on the contractile power of the heart muscle, and that slowing of the heart-rate need not be produced. The most striking results occur in fibrillation, when the rate is rapid because slowing is produced. If the heart-rate is between 70 and 80, the conditions are closer to those with normal rhythm.

RESULTS OBTAINED IN THIS SERIES

There were 47 patients, 36 males and 11 females, on whom 58 tests on digitalis effect were carried out. In the great majority (42 of 47) the failure was moderate or great on admission. The patients were divided into five groups and the group distribution is indicated in Table I.

For purposes of comparison there were 30 cases of failure with auricular fibrillation on whom 32 tests were made. Again the majority (22 in 30) were in moderate or great failure on admission. As expected, the association being rare, there were no syphilitic cases with fibrillation. Unlike the normal rhythm series where each aetiological group (except Group 5) is well represented, almost half the fibrillating cases were rheumatic.

TABLE I
RESULTS OF DIGITALIS TREATMENT IN HEART FAILURE (1) WITH
NORMAL RHYTHM, AND (2) WITH AURICULAR FIBRILLATION
NORMAL RHYTHM

GROUP	BASIS OF FAILURE	NUMBER OF PATIENTS	NUMBER OF TESTS	CLINICAL IMPROVEMENT (IN TESTS)	REDUCTION IN RATE (IN TESTS)
1.	Hypertension	25	32	19	14
2.	Hypertension and past Coronary Thrombosis				
3.	Chronic Rheumatic Val- vular Disease.	11	14	10	7
4.	Syphilitic Heart Disease.	9	10	5	6
5.	Unclassified.	2	2	1	0
	Total	47	58	35	27
	Percentage of Tests ..			60.3%	46.5%

TABLE I—continued
AURICULAR FIBRILLATION

GROUP	BASIS OF FAILURE	NO. OF PATIENTS	NO. OF TESTS	CLINICAL IMPROVEMENT (IN TESTS)	REDUCTION IN RATE (IN TESTS)
1.	Hypertension	12	14	9	10
2.	Hypertension and past Coronary Thrombosis				
3.	Chronic Rheumatic Valvular Disease.	14	14	12	14
4.	Syphilitic Heart Disease	0	—	—	—
5.	Unclassified.	4	4	2	4
Total		30	32	23	28
Percentage of Tests ..				71.9%	87.5%

The good effect of rest in bed without other treatment is discussed later, the influence of this on the pulse-rate, weight, and balance of fluid intake and urinary output in one patient is shown here in Fig. 1.

Of the 58 tests on digitalis effect in normal rhythm, 35 (60%) were successful, there being 17 (29%) with slight benefit and 18 (31%) with moderate or great benefit. Only 7 (12%) showed striking improvement and a composite chart is given of four of them (Fig. 2). In this chart the dose is given as gr. ii, t.i.d. correctly for three of the cases, but the fourth had gr. iii, t.i.d. ; a similar

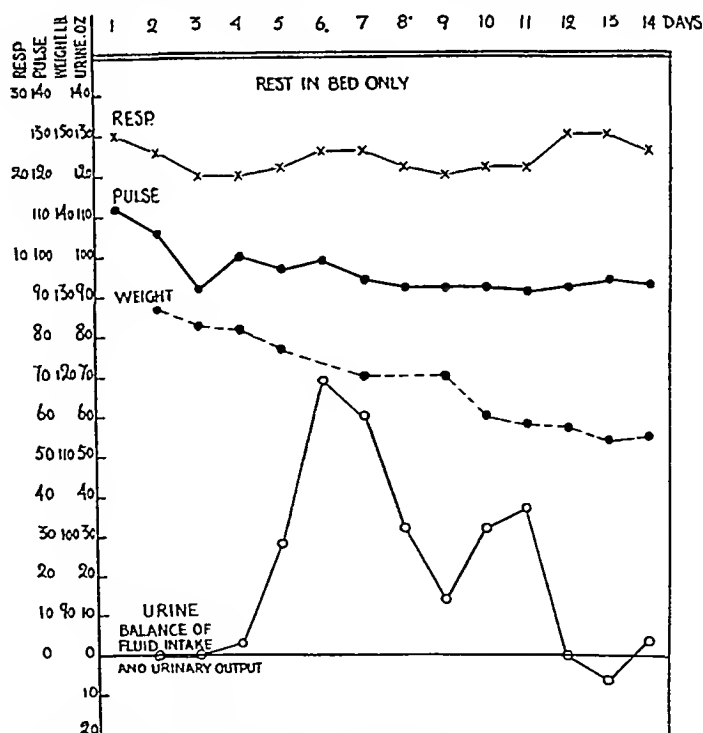


FIG. 1.—Effect of rest in bed alone in heart failure with normal rhythm. Woman, aged 52, with hypertensive heart disease, gross œdema, and hydrothorax.

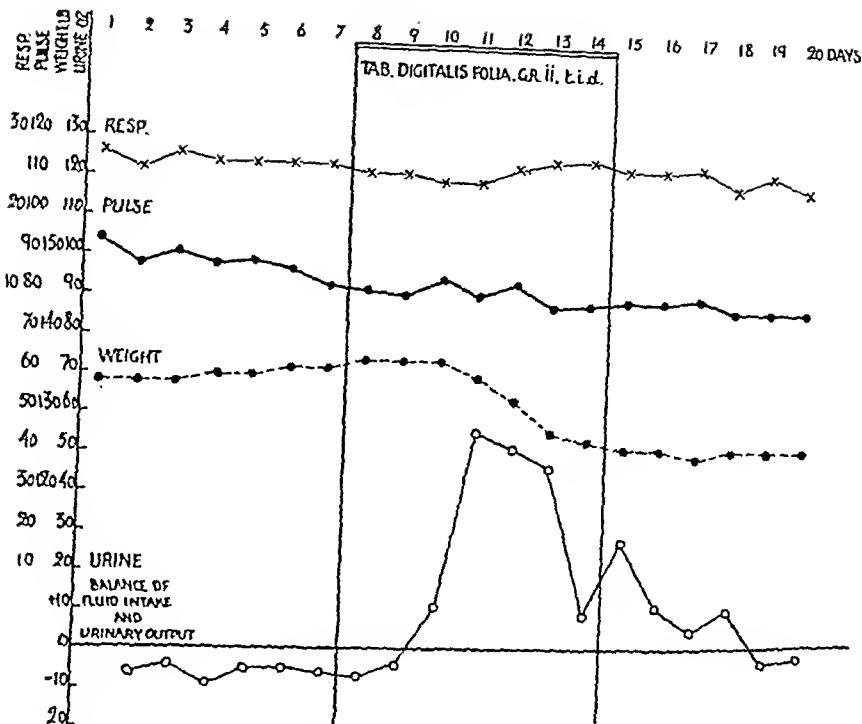


FIG. 2.—Effect of digitalis in heart failure with normal rhythm. A composite chart from four severe cases, all with œdema.

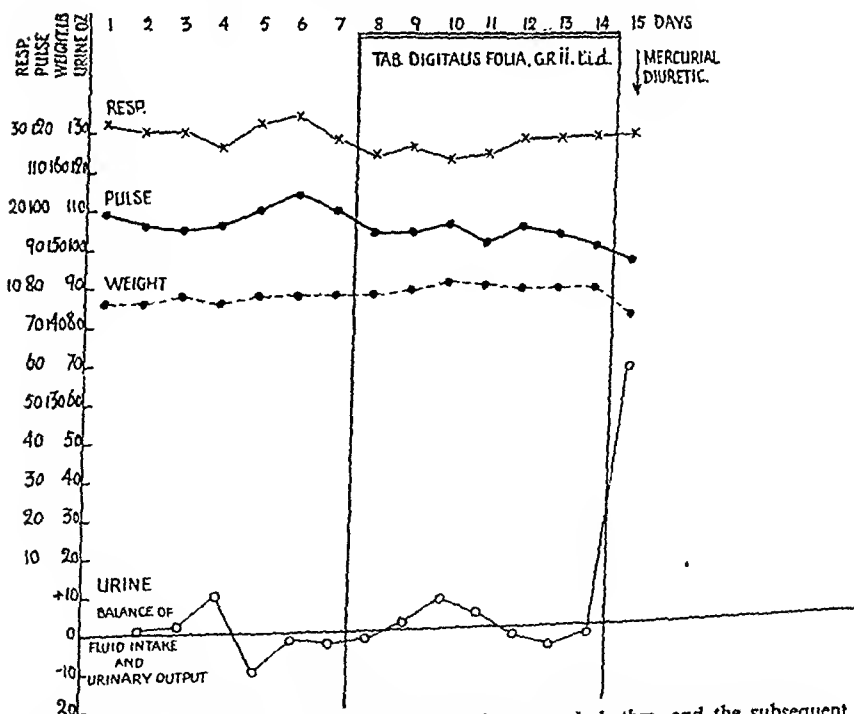


FIG. 3.—Absence of effect of digitalis in failure with normal rhythm, and the subsequent effect of a mercurial diuretic. A composite chart from four severe cases, all with œdema.

exception holds for Fig. 3, which shows the complete ineffectiveness of digitalis in four cases. These results are rather disappointing, especially with regard to the infrequency of striking benefit, for only about one in eight patients in failure with normal rhythm can be expected to respond thus well. Nevertheless the majority benefit to some extent and would probably benefit more from administration over long periods.

In the series with auricular fibrillation, some degree of benefit from digitalis was seen more often, though not much oftener than in normal rhythm (72% against 60%). The incidence of great improvement was however more than twice that in normal rhythm (28% against 12%).

Diuresis occurred in about half of all test courses in normal rhythm (27 in 58); it was moderate in eight and striking in six (10.3%). The majority (24 of 35) of the observations with benefit were, as expected, accompanied by diuresis.

In auricular fibrillation diuresis occurred in 14 of 32 tests, much as in normal rhythm. Diuresis was moderate in eight and striking in four (12.5%). Of 23 with benefit, 16 showed diuresis.

Successive Courses of Digitalis in the Same Individual.—When a patient in failure with normal rhythm benefits from digitalis on a first occasion, he is likely to respond again when in failure some weeks or months later: six of eight patients responded thus. If digitalis fails at the first test, it does not follow that it will fail again; indeed, of four failing to respond at the first, two responded at a second test when again in failure.

FACTORS WHICH MAY INFLUENCE DIGITALIS RESPONSE

(a) *Rest in Bed.*

The effect of rest in bed during the control period was evaluated in the 47 cases with normal rhythm. Benefit occurred in 17 (about 40%); in 9 it was moderate or great, and in 1 of these it was outstanding (Fig. 1). Nine patients, six of them with hypertension, became worse during the rest period. Of these nine, five were considerably improved by digitalis, in three the immediate downward trend of failure was arrested, while the remaining patient became worse on digitalis and died.

Mackenzie (1911) and Janeway (1913) having drawn attention to the effect of rest, most subsequent investigations on digitalis have been controlled in this way. But rest also remains a factor in enhancing digitalis effect during the course. If progress has not become stationary on rest alone, then the "rate of progress" (Luten, 1924) becomes important when assessing the benefit from digitalis.

Contrary to what was expected, benefit from rest in bed was only a little less frequent in the fibrillating cases. All the seven patients (four in the rheumatic group) who deteriorated on rest in bed benefited from digitalis.

ing the recurrence of failure. No one claims that digitalis has the same value either in controlling rate or in warding off failure when the rhythm is normal ; though it should, of course, be used with these objects in view.

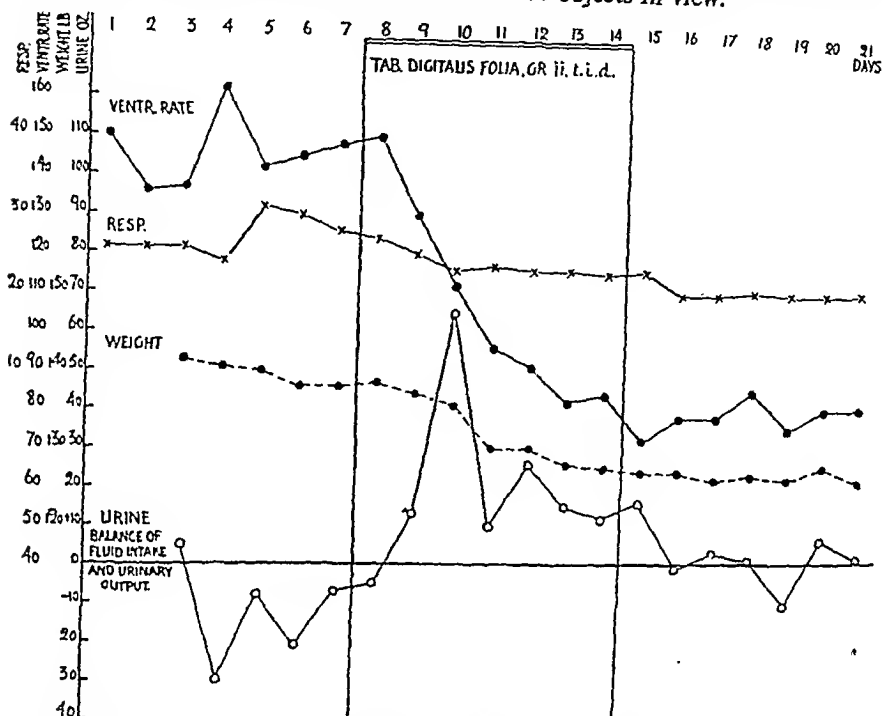


FIG. 4.—Effect of digitalis in rheumatic heart failure with auricular fibrillation. Woman aged 64 with mitral stenosis, great œdema, and hydrothorax

(d) *Œdema.*

We included cases without demonstrable œdema at the end of a control period (most had œdema on admission), provided there remained ample evidence of failure ; and digitalis was by no means without effect upon them. In fact, considerable benefit was obtained as often without as with œdema, and some response occurred in 75 per cent. without œdema against 52 per cent. with œdema. Figures for the fibrillation series ran parallel.

Though with normal rhythm considerable diuresis was twice as common in patients with œdema, yet some diuresis was not uncommon without œdema, 6 in 16. Thus we cannot go so far as some (Hay, Jones, and Ince, 1927) who have stated that no œdema means no diuresis. In patients with cardiac failure, several pints of fluid may be retained in the tissues before œdema becomes manifest, and a digitalis diuresis reveals what has really been latent.

In the auricular fibrillation series without œdema, considerable diuresis was even more common than in normal rhythm without œdema (6 in 12 against 2 in 16).

(e) *Hydrothorax. Respiratory Rate.*

There were 13 normal rhythm cases with hydrothorax ; in six it was on the right, in four on the left, and in three bilateral. The rheumatic group was not represented ; syphilitic heart disease accounted for three (one right, two left) ; and the remainder were in the two hypertension groups. Digitalis dispelled the hydrothorax in five and reduced it in one. Though the hydrothorax was not appreciably affected in three patients, they derived benefit from the drug in other directions, e.g. loss of œdema. Patients with hydrothorax responded like those without.

It was remarked that even with hydrothorax the charted rate of respiration immediately before digitalis was in some cases as low as 20, the average being 25, as it was also in severe failure without hydrothorax. With improvement on digitalis the respiratory rate usually fell, though the average fall was only two or three ; sometimes there was no fall (Fig. 2).

In five cases of auricular fibrillation with right hydrothorax, digitalis was effective, the hydrothorax being dispelled completely in two and reduced in one.

Thus in severe failure, whatever the rhythm, digitalis is as likely to benefit a patient with a hydrothorax as one without.

(f) *The Duration of Incapacity.*

It might have been thought that in cases with normal rhythm and failure of short standing (under 6 months), the immediate results from digitalis would be better than in those of longer standing, but this idea was not supported by our figures, any more than the idea that patients in a first failure would respond better than in a subsequent failure. The same observations apply to auricular fibrillation.

(g) *The Severity of Failure.*

This did not much matter in deciding whether digitalis would act or not. Fourteen of 20 tests in slight failure and 17 of 38 in moderate or great failure were successful. In fibrillation the proportions were 8 of 12 in slight failure, and 15 of 20 in moderate or great failure.

The superiority of digitalis in auricular fibrillation is most evident if the severer grades of failure are alone considered. Only 7 of 38 in normal rhythm responded brilliantly, but no fewer than 9 of 20 in auricular fibrillation.

(h) *Age and Prognosis.*

The age factor arises chiefly in relation to ætiology. The rheumatic cases with normal rhythm were on an average 22 years younger and the syphilitic group on an average 8 years younger than the hypertension groups, where the average age was 61. The age factor proved to be of little importance, though the tendency was for a decline in digitalis response as age advanced. Yet among those aged 65 to 70, no fewer than five of nine patients responded and two of them well.

The pathological basis of failure could not be correlated with the likelihood of digitalis response. In auricular fibrillation, however, the incidence of benefit was far greater in the rheumatic group than in the non-rheumatic groups, and this has been discussed above, under 'c'.

We thought it likely that in patients with normal rhythm, whose survival-period proved to be under one year, digitalis might be less effective. This did not prove to be the fact, for of 18 patients who died within a year, 10 had benefited from digitalis and 8 had not. Moreover, of four who died within a few weeks of uncomplicated heart failure (proved at necropsy in three), two responded well to digitalis, a proportion not very different from those with a better prognosis. There was no essential difference in the death rate between the ætiological groups in normal rhythm, and we know that 18 of 29 patients who were followed up to July 1938 died within a year.

Comparison of Digitalis Effect during Normal Rhythm and during Auricular Fibrillation in the Same Individual.—There were five such cases, in two of which the fibrillation was produced or more likely precipitated by digitalis. It happened that the average rate was the same in normal rhythm as in auricular fibrillation, i.e. 88. Under digitalis during normal rhythm, the rate fell to 81, while during auricular fibrillation the rate fell to 66 : a fall of 7 and 22 respectively. As to clinical benefit, we have adequate observations on four of them, and in two digitalis failed both in normal rhythm and in auricular fibrillation. In the other two digitalis gave a better clinical result when fibrillation obtained.

Digitalis and Mercurial Diuretics

When a course of digitalis failed, a mercurial diuretic was often given. In 16 such cases with normal rhythm it invariably produced a diuresis ; it never failed even where œdema was absent, though naturally the greatest response was in the œdematous. The previous administration of digitalis appeared to make no difference to the diuretic response, and this confirms the experience of Thomson (1937). Fig. 3 shows the good effect of a mercurial diuretic in four patients who had not been helped by digitalis.

Salyrgan is more than an adjuvant in failure with œdema, but it does not meet the inherent difficulty—myocardial insufficiency. At the best a mercurial diuretic simply removes collected and stagnant fluid and thereby relieves the patient. Digitalis acts often enough under observation, as we have shown, to make it likely that more prolonged use in adequate doses will extend improvement and postpone relapse.

Subsidiary Groups (6-10)

These groups comprising 18 patients (22 tests) with normal rhythm are separately considered for reasons obvious in the diagnosis.

Group 6. Congenital Heart Disease ; three cases, three tests.

Two patients, aged 63 and 11, had Fallot's tetralogy. Both responded slightly to digitalis. The remaining patient, aged 43, with coarctation of the aorta, was not improved.

Group 7. Rheumatic Carditis with Valvular Disease ; seven cases, nine tests.

The average age was only 17. All had considerable œdema. A single patient improved on digitalis and two others showed a reduction in rate from an average of 125 to 97. Six died later, four within a few months and two within two years.

Group 8. Infective Endocarditis ; three cases, four tests.

Post-mortem proof of the diagnosis was obtained in all three cases. In a single patient digitalis increased the urinary output with slight temporary benefit, but no effect at all was demonstrable in the others.

Group 9. Complete Heart-block ; two cases, two tests.

Both patients had slight œdema. One improved with a diuresis and a slight fall in ventricular rate from 32 to 27 ; the other was unaffected.

Group 10. Chronic Nephritis ; three cases, four tests.

All had cardiac failure. In the one patient without œdema, digitalis relieved the dyspnœa and abolished Cheyne-Stokes respiration and pulsus alternans. The other two patients, with œdema, improved and showed diuresis.

SUMMARY AND CONCLUSIONS

1. This investigation was undertaken primarily to decide the clinical value of digitalis in heart failure with normal (sinus) rhythm. The secondary purpose was to compare its value in such failure with that in auricular fibrillation, which is better known.

2. Sixty-five patients with heart failure and normal rhythm were observed. After one week or more at rest in bed, digitalis leaf was given in a dose of 2 grains three times a day, i.e. 6 grains (0.4 g.) daily, for one to two weeks. The condition at the beginning of digitalis treatment was compared with that at the end. The criteria of failure were dyspnœa, liver enlargement, and œdema with or without hydrothorax ; and judgment as to improvement was made on these criteria together with diuresis. Reduced heart-rate was not reckoned as a criterion, and it is separately considered. Twenty-five patients had hypertensive heart disease, 12 with and 13 without past coronary thrombosis ; 11 had chronic rheumatic valvular disease ; 9 had syphilitic heart disease ; and 2 were unclassified. In these, the main groups, the majority, 72 per cent., had œdema at the end of the week's rest in bed and a quarter of these had hydrothorax, confirmed by X-ray examination.

3. The control lay in the preliminary rest in bed without digitalis ; but for comparison another series of 30 patients with failure and auricular fibrillation was observed in the same way.

4. Under rest in bed only, in normal rhythm, 17 of 47 (36%) improved ; in auricular fibrillation, 11 of 28 (39%) improved.

5. The main digitalis results are shown in Table I and there are illustrative charts of effect and of failure of effect. In normal rhythm some clinical improve-

ment was demonstrated in 35 out of 58 tests (60%) ; and 23 of 58 showed none. Admittedly 17 received only slight benefit, so that moderate or great benefit resulted in 18 only, i.e. 31 per cent. of the whole. There was little difference in response among the separate ætiological groups, though the rheumatic group responded best (Table I).

The heart-rate in failure with normal rhythm is moderate, the average in our series before digitalis being 85. It was reduced by digitalis in 27 out of the 58 tests (47 patients), i.e. in almost half (46·5%). The average fall in rate among those in whom it occurred was from 85 to 67, i.e. 18. This was usually secured without toxic symptoms, and when these appeared (20%) they were slight (nausea and rarely vomiting). Whatever the initial rate, digitalis often reduced it. Reduction in rate was not always accompanied by clinical improvement, though improvement was rather more common in the patient who showed it. Some good clinical results were seen without any reduction in rate (Table II).

Diuresis was induced by digitalis in 27 of 58 tests (47 patients) in normal rhythm. It was freer in patients with gross œdema than in those with little or none ; but some diuresis was obtained almost as frequently in those without as in those with œdema.

The course of the disease after the onset of failure in normal rhythm is short—18 of 29 patients died within a year—and this in general must lessen the likelihood of improvement from digitalis. Yet in a particular patient the response to digitalis is no guide to the expectation of life ; and if digitalis fails at a first trial, it may occasionally succeed at a later trial.

6. Of the patients with *auricular fibrillation*, 12 had hypertensive heart disease, 14 had chronic rheumatic valvular disease, and 4 were unclassified. Clinical improvement was demonstrated in 23 of 32 tests (30 patients), i.e. in 72 per cent. ; and 9 showed none. It was slight in nine, and moderate or great in fourteen, i.e. 44 per cent. of the whole.

The heart-rate was higher than in the normal rhythm series, an average of 98 against 85, a difference of 13. The rate was reduced by digitalis in the great majority, in 28 of 32 tests (87%). The average fall in rate where a fall resulted was from 100 to 70, an average fall of 30. Most of those with slowing also showed benefit, but in the absence of slowing there was none.

The rheumatic group was distinguished by a higher average rate before treatment, by reduction of the rate in all fourteen cases, and by clinical improvement in all but two. Even with a moderate initial rate (below 100), results were better in rheumatic than in non-rheumatic fibrillation, though no better than in rheumatic cases with normal rhythm.

Without the rheumatic group, the fibrillation series responded to digitalis no better than the normal rhythm series. In hypertension, for instance, the results were similar.

7. A mercurial diuretic sometimes administered after a digitalis test nearly always produced a free diuresis even where digitalis had failed. In œdematous patients other than those with rheumatic auricular fibrillation and a high ventricular rate, a mercurial diuretic usually has more value than digitalis. Yet a trial of digitalis cannot be omitted, for it alone acts directly on the heart.

The partnership of a mercurial diuretic with digitalis should govern the treatment of heart failure.

8. Digitalis is always indicated in congestive heart failure irrespective of rhythm, but it is often inefficient, as it fails completely in about a third of all cases.

In heart failure with normal rhythm digitalis is helpful in rather more than half the cases.

In heart failure with auricular fibrillation, digitalis is more often helpful than it is in normal rhythm, for it benefits more than two-thirds. This superiority rests on its particular value in rheumatic heart failure with fibrillation, largely but not entirely due to the high ventricular rate. Incidentally, it is in this group that rate control by continued digitalis best prevents recurrence of the failure.

The real difference in the response of heart failure to digitalis lies not between auricular fibrillation and normal rhythm, but rather between rheumatic auricular fibrillation and all other kinds of heart failure irrespective of rhythm.

We are indebted to Drs. C. Hollins, R. W. Parnell, and F. S. Cosh, house physicians to the Cardiac Department, for their great assistance in recording clinical observations; and to the Sisters of the Wards for their valued co-operation. Dr. John Grimshaw has kindly advised us on the text.

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PRÆCORDIAL LEADS IN ELECTRO-CARDIOGRAPHY

From the early days of electrocardiography, attempts to understand the cause of the various waves have been made by the use of leads on different parts of the surface of the heart. This method has not been available for use in man, and clinical study has been mainly confined to the three standard leads, the appearance of which has now become familiar to all. More recently leads from various points over the chest wall have been used and many valuable papers have been published. Unfortunately different conventions have been adopted for placing the electrodes so that comparisons have been difficult, and in some cases the normal curves have shown inverted T waves and in others upright T waves, with corresponding changes in the other complexes. It is not yet certain if the fourth lead, or still other leads, will become essential in routine clinical work, but it is certain that they help greatly in understanding what is taking place in the heart. It is, therefore, important that all these should be as easy to compare as possible and intelligible to as wide a circle as possible.

At the first General Meeting of the Cardiac Society of Great Britain and Ireland, held at Edinburgh on April 15, 1937, Dr. John Cowan proposed that a committee should be appointed to see if it was possible to reach agreement on the points to be adopted for a standard lead IV. This was approved, and fortunately the American Heart Association had already appointed a committee for the same purpose. It proved possible for the two to reach agreed conclusions, embodied in the following memorandum. This was published in the *British Medical Journal* and in the *Lancet* on January 22, 1938, and at the same time in America ; but it seems desirable to reprint it in this Journal, partly for convenience and partly as a record of the work of the first committee appointed by the Cardiac Society.

A JOINT MEMORANDUM

At the request of the Council of the Cardiac Society of Great Britain and Ireland we print below a Memorandum on Præcordial Leads in Electrocardiography. Many different positions have been used for the electrodes in obtaining these electrocardiograms, and much confusion has arisen from the different methods in use. As it has been possible for the Cardiac Society of Great Britain and Ireland and the American Heart Association to reach agreement it is hoped that these joint recommendations will be useful, both to those working at the subject and to all others who are interested.

RECOMMENDATIONS FOR STANDARDIZATION

In the last few years electrocardiographic leads in which an electrode placed upon the præcordia is paired with an electrode in contact with some part of the body distant from the heart have come into widespread use. The confusion which has resulted from the lack of uniformity and precision in the technique and nomenclature employed by different observers in connexion with leads of this kind has led to an almost universal desire that a standard practice be established. To this end the Cardiac Society of Great Britain and Ireland and the American Heart Association have each appointed a committee to consider this matter and make recommendations. The two committees have conferred and have agreed jointly to make recommendations with reference to the routine use of a single præcordial lead. It is understood that either committee may make additional reports with reference to multiple præcordial leads and other matters not dealt with in the present report.

1. It is recommended that those who employ a single præcordial lead place the præcordial electrode upon the extreme outer border of the apex beat, as determined by palpation. If the apex beat cannot be located satisfactorily by palpation the electrode may be placed in the fifth intercostal space just outside the left border of cardiac dullness, or just outside the left mid-clavicular line if percussion of the heart is unsatisfactory. Where præcordial leads are taken by a technical assistant, the position for the præcordial electrode should be marked on the chest by the physician.

2. It is recommended that a single præcordial lead in which the præcordial electrode has the location specified in the preceding paragraph be known as lead IV B when this electrode is paired with an electrode in the left interscapular region ; lead IV R when it is paired with an electrode on the right arm ; lead IV L when it is paired with an electrode on the left arm ; lead IV F when it is paired with an electrode on the left leg ; and lead IV T when it is paired with a central terminal connected through equal resistances of 5,000 or more ohms to electrodes on each of the three extremities mentioned.

It is suggested that for all ordinary purposes lead IV R or lead IV F be employed. The latter lead should have the preference until it has been established that the former, which is somewhat more convenient, is equivalent to the latter for all practical purposes, or yields results of equal value.

3. It is recommended that in taking the præcordial leads specified the galvanometer connexions be made in such a way that relative positivity of the apical electrode is represented in the finished curve by an upward deflection (a deflection above the iso-potential level) and relative negativity of the apical electrode by a downward deflection. It is urged that this convention be adhered to in the case of præcordial leads other than those specified, and also in the case of all leads in which one electrode is placed much closer to the heart than the other. In other words, it shall be the standard convention in taking such leads to make the galvanometer connexions in such a way that relative positivity of the electrode nearer the heart is represented by an upward deflection.

4. It is recommended that with the galvanometer connexions made as described in the preceding paragraph the deflections of præcordial leads be designated by the symbols P, Q, R, S, and T, and that in the application of these symbols the same conventions be employed as in the case of the standard limb leads.

5. It is recommended that in taking præcordial leads the electrocardiograph be so adjusted that a deflection of 1 cm. in the finished record corresponds to a potential difference of one millivolt, as in the case of the standard limb leads. Any reduction in sensitivity made necessary by very large deflections should be clearly indicated on the curve, preferably by photographing the effect of introducing a potential difference of 1 mv. into the galvanometer circuit.

6. It is recommended that the greatest dimension of the apical electrode employed in taking the leads specified in this report be 3 cm. or less. A circular electrode between 2 cm. and 3 cm. in diameter should ordinarily be employed.

7. It is recommended that the terms lead IV (R, F, etc.), apical lead, apex-leg lead, etc., be used henceforth only in connexion with the leads specified in this report.

The above recommendations have been drawn up by the following two committees, working in co-operation :

Committee of the Cardiac Society of Great Britain and Ireland

D. Evan Bedford (London)

John Cowan (Glasgow)

A. N. Drury (Cambridge)

I. G. W. Hill (Edinburgh)

John Parkinson (London)

P. H. Wood (London)

Committee of the American Heart Association

Arlie R. Barnes (Rochester)

Harold E. B. Pardee (New York)

Paul D. White (Boston)

Frank N. Wilson (Ann Arbor)

Charles C. Wolferth (Philadelphia)

These joint recommendations have been approved by the Council of the Cardiac Society and by the American Heart Association, who now authorize their publication. The following addendum to the joint report has been made by the Cardiac Society.

ADDENDUM BY CARDIAC SOCIETY

1. The above report deals with the nomenclature and technique for obtaining a single præcordial lead suitable for routine clinical work. The committee of the Cardiac Society had insufficient evidence available to permit their making recommendations in respect of multiple præcordial leads. The American

Heart Association will, however, draw up such recommendations, and, when published, copies of these will be available for those specially interested on application to the secretary of the Cardiac Society (Dr. Maurice Campbell, 25, Upper Wimpole Street, London, W.1).

2. In using either of the two standard præcordial leads—for example, lead IV R or lead IV F—the correct polarity (paragraph 3) is obtained as follows. The lead switch is turned to lead I. The L.A. terminal is connected to the præcordial electrode. The R.A. terminal is connected to the distant electrode—for example, to the right arm for lead IV R, or to the left leg for lead IV F.

CHEST LEADS IN CLINICAL ELECTRO-CARDIOGRAPHY

BY

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In a previous communication Sorsky and Wood (1937) presented the normal appearances of chest lead electrocardiograms, paying particular attention to normal variations and to the position of the proximal electrode. As the question of standardizing the technique for chest leads was then under consideration by the Cardiac Society of Great Britain and Ireland and the American Heart Association, further work was held up pending their conclusions, which have now been published (1938). On the question of polarity it was agreed that the galvanometer connections should be so arranged that relative positivity of the proximal electrode yields an upward deflection on the electrocardiogram. By lead IV is meant a chest lead in which the proximal electrode is placed upon the apex beat. When this is paired with the right arm it is called lead IV R, and when it is paired with the left leg it is called lead IV F. In all our work we have connected the proximal electrode to the left arm terminal, so that lead IV R is obtained by setting the lead selector dial on the electrocardiograph to lead I, and lead IV F by setting this dial to lead III, after interchanging the terminals in order to correct the polarity.

In our previous work on 150 normal controls, our description of the normal variations of the chest lead electrocardiogram was in terms of the opposite polarity to that now accepted, and based on chest leads paired with the left leg. It is now necessary to refer to our records of chest leads paired with the right arm, in which the accepted polarity was obtained. From an analysis of these electrocardiograms we may present the normal appearances of lead IV R as follows :

1. The P wave is upright and averages 0.14 mv. in amplitude, with a maximum of 0.25 mv.
2. A Q wave is present in 22 per cent. and averages 0.15 mv. in amplitude with a maximum of 0.5 mv.
3. The main QRS deflection is upright and is never monophasic. R is very tall and S averages 0.75 mv.
4. The RS-T segment usually lies at the iso-potential level, but it may be elevated to a maximum of 0.1 mv., or rarely it may be slightly depressed.

5. The T wave is always upright and averages 0.7 mv. in amplitude, ranging between 0.3 and 1.4 mv.

Lead IV F is similar except that the P wave is usually diphasic or inverted and is often very small. Typical records are shown in Fig. 1 (A and B).

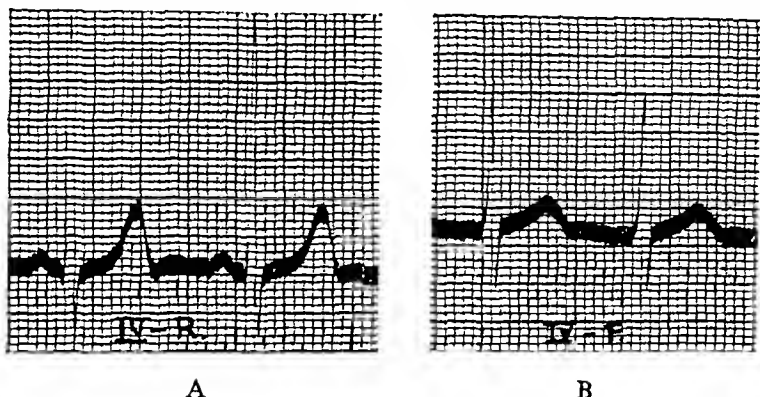


FIG. 1.—Normal chest-lead electrocardiograms. (A) Lead IV R. (B) Lead IV F.

In addition to leads IV R and F we have studied four other chest leads : (1) the left pectoral—right arm lead ; (2) the left pectoral—left leg lead ; (3) the right pectoral—right arm lead ; (4) the right pectoral—left leg lead. In the right pectoral leads the proximal electrode was placed in the fourth intercostal space at the right border of the sternum ; in the left pectoral leads it was placed midway between this point and the apex * (see Fig. 2).

In normal controls it was found that in the apical leads the R deflection dominated the QRS complex, but that shifting the proximal electrode to the right favoured the S deflection, so that in the left pectoral leads R and S were more or less of equal amplitude, and in the right pectoral leads S was the dominant deflection. This phenomenon is illustrated in Fig. 3A, and was found in 75 per cent. of the controls when the proximal electrode was paired with the right arm, and in 95 per cent. when the proximal electrode was paired with the left leg.

The effect upon the T wave of shifting the proximal electrode to the right differed according to the distal electrode employed. When the right arm was used the T wave remained upright even in the right pectoral lead. But when the left leg was used the T wave often became inverted. Thus in the left pectoral—left leg lead the T wave was inverted in 21 per cent. of normal children and occasionally in slim young adults, and in the right pectoral—left leg lead it was inverted in 65 per cent. of normal children and in 58 per cent. of normal adults (see Table I). An electrocardiogram showing inversion of the T waves in the left and right pectoral—left leg leads in a normal child is shown in Fig. 3B.

* In the terminology recommended by the American Heart Association, our right pectoral—right arm lead would be called lead CR 1, and our left pectoral—right arm lead, though it has no exact counterpart, corresponds roughly to lead CR 3.

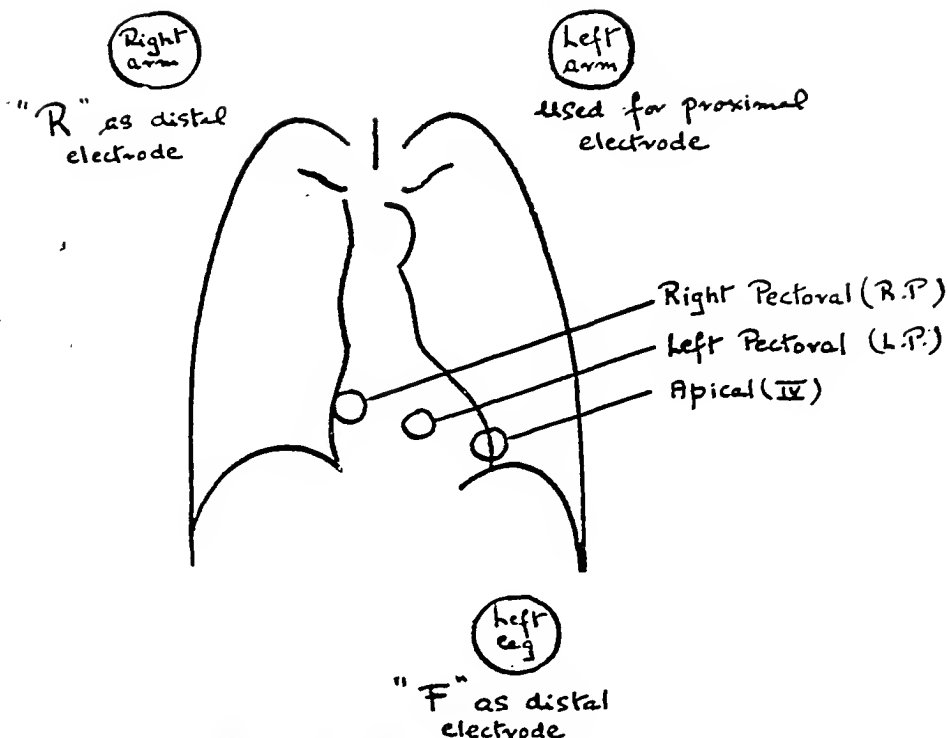


FIG. 2.—Diagram showing positions of the proximal electrode in relation to the underlying heart.

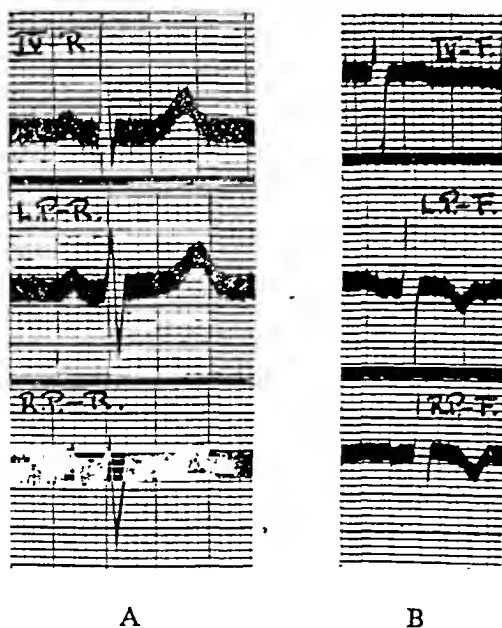


FIG. 3.—Normal chest leads showing the behaviour of the QRS complex (A), and of the T wave in a child (B), as the proximal electrode is shifted from the apical (top) to the left pectoral (middle) and to the right pectoral (bottom) position.

TABLE I
INVERSION of the T WAVES in PECTORAL LEADS
PAIRED WITH THE LEFT LEG

	LEADS		
	IV-F	L.P.-F.	R.P.-F
CHILDREN	RARE	21 %	65 %
ADULTS	NIL	RARE	58 %

The present report deals with the chest lead electrocardiograms obtained from 314 patients selected for different purposes. No case was included in which the diagnosis was in doubt. In the majority nine tracings were taken, three with limb leads and six with chest leads. Serial records were obtained in about a third of the cases, particularly in those which we thought might show transient changes. Many graphs were discarded because of uncertainty of diagnosis or because of mixed etiological factors. The total number of chest lead tracings taken has been estimated at 3,000, excluding normal controls. The object of the work was twofold : to determine the best distal electrode ; and to assess the value of multiple chest leads. This necessitated a wide investigation into the value of chest leads in general and in all types of heart disease. The material is analysed in Table II.

TABLE II
MATERIAL
314 SELECTED CASES

ACTIVE RHEUMATIC CARDITIS	30
PERICARDITIS	7
LEFT VENTRICULAR ENLARGEMENT	120
CARDIAC DISPLACEMENT	12
RIGHT VENTRICULAR ENLARGEMENT	50
BUNDLE BRANCH BLOCK	20
DIGITALIS EFFECT	15
MYOCARDIAL INFARCTION	33
ANGINA PECTORIS	27

Cases of thyrotoxicosis, bacterial endocarditis, and of congenital heart disease without cardiac enlargement produced no special electrocardiographic changes with limb or with chest leads, and have not been included in this series.

Cases of aortic valvular disease of any etiology have been grouped with cases of hypertensive heart disease under the heading of left ventricular enlargement if that was present, and cases of mitral stenosis, pulmonary stenosis, and cor pulmonale have been grouped together under the heading of right ventricular enlargement unless there was evidence to the contrary. We also studied thirty cases of severe anæmia, five of myxoedema, and one case of toxic myocarditis from pneumonia. Chest leads proved of no help in the diagnosis of these conditions, the changes in both limb leads and chest leads being of a similar order.

RHEUMATIC CARDITIS

Electrocardiographic evidence of rheumatic carditis is more or less confined to prolongation of the P-R interval, to nodal rhythm, heart block, and to bundle branch block, i.e. to conductive defects. Alterations in the RS-T segment or in the T wave in limb lead electrocardiograms are usually due to pericarditis. It has been stated, however, that changes in the T wave may occur with chest leads. Thus Levy and Bruenn (1935) found frequent alterations in the direction and voltage of the T wave in serial chest lead records in cases of rheumatic carditis. Their results have already been criticized (Sorsky and Wood, 1937) on the grounds that normal children frequently show reversal of the T wave in the lead which they used. Robinow, Katz, and Bohning (1936) made a more careful study of cases of rheumatic carditis, checking their findings against a group of normal controls, and they concluded that reversal of the T wave in chest leads was more common in children with rheumatic carditis than in normal children.

It must be remembered that reversal of the T wave is found in the left pectoral—left leg lead in 21 per cent. of normal children, and that the T wave is diphasic in this lead in another 18 per cent. (Sorsky and Wood, 1937). We wish to emphasize the fact that such reversal of the T wave rarely occurs if the proximal electrode is paired with the right arm, or if it is placed on the apex beat and not within it.

Bearing these facts in mind we have analysed the chest-lead electrocardiograms of thirty cases of active rheumatic carditis, excluding those with pericarditis. In many serial records were obtained.

The QRS complex was always normal. The RS-T segment did not deviate from the iso-potential level. There were, however, changes in the direction of the T wave in some instances. When the proximal electrode was paired with the right arm the T wave was inverted in three cases in the apical lead, in three cases in the left pectoral lead, and in ten cases in the right pectoral lead; when the proximal electrode was paired with the left leg the T wave was inverted in five instances in the apical lead, in ten instances in the left pectoral lead, and in twenty in the right pectoral lead. These figures are expressed per cent. in Table III. If the T wave was inverted in the apical or in the left pectoral lead, it was also inverted, and usually more so, when the proximal electrode was shifted to the right. This rule is always obeyed by normal controls, and it will

be shown later that it also holds good for cases with right ventricular stress or enlargement. The above figures show that the T wave is more often inverted in children with rheumatic carditis than in normal children. When the proximal electrode is paired with the right arm inversion of the T wave is more significant though less common than when it is paired with the left leg.

It is concluded that chest leads may be of value as an aid in the diagnosis of active rheumatic carditis ; that this value is enhanced if the proximal electrode is paired with the right arm, and is reduced if it is paired with the left leg ; that the changes consist of inversion of the T wave, and occur least in the apical lead and most frequently in the right pectoral lead ; that if there is inversion of the T wave in any lead there is usually less inversion if the proximal electrode is shifted to the left and more inversion if it is shifted to the right ; and finally that, as will be shown subsequently, these changes are similar to those produced by stress or enlargement of the right ventricle from any cause, so that it is possible that the changes of rheumatic carditis merely represent right ventricular stress.

TABLE III
INVERSION of the T WAVE
IN CASES of RHEUMATIC CARDITIS

CHEST LEAD	R.	F.
IV	10 %	16.6 %
LEFT PECTORAL	10 %	33.3 %
RIGHT PECTORAL	33.3 %	66.6 %

PERICARDITIS

Wood (1937) has recently described the changes in limb lead electrocardiograms in cases of pericarditis as being of a T_2 pattern, both the early elevation of the RS-T segment and the later inversion of the T wave being maximum in lead II.

Vander Veer and Norris (1937) showed illustrations of chest lead tracings in four cases of pericarditis which exhibited typical changes of a T_2 pattern in serial limb leads. For some reason these chest lead tracings were quite normal, and the authors concluded that the electrocardiographic changes of pericarditis could be distinguished from those of myocardial infarction by the fact that the former did not occur in chest leads. At the time of their publication we knew that this conclusion was incorrect, and since then Bellet and McMillan (1938) have reported marked changes in chest leads in cases of pericarditis. Using the old polarity they found initial depression of the RS-T segment and later reversal of the T wave. These changes often lasted longer than those in the limb leads. In some cases they found that the abnormality in the chest lead

only appeared when the proximal electrode was placed over the area of pericardial friction.

We used chest leads in seven cases of pericarditis, six of which exhibited limb lead changes of the T_2 pattern. Two were rheumatic, two malignant, on tuberculous, one infective, and one was a case of chronic constrictive pericarditis. An effusion was present in five of them. Only one showed elevation of the RS-T segment in the early phase in limb leads, and this elevation was more evident in the chest leads. Inversion of the T wave occurred in all cases in the apical and in the left pectoral leads, and usually in the right pectoral leads as well, and were equally evident with either distal electrode. Of the seven cases, two came to autopsy and two were chronic, so that the changes during the period of recovery were only studied in three; limb leads were normal in one, and inverted T waves persisted longer in chest than in limb leads in the other two. The degree of T wave inversion was greater in chest leads, and the form of the QRS complex was always normal. These facts are illustrated in Figs. 4 and 5.

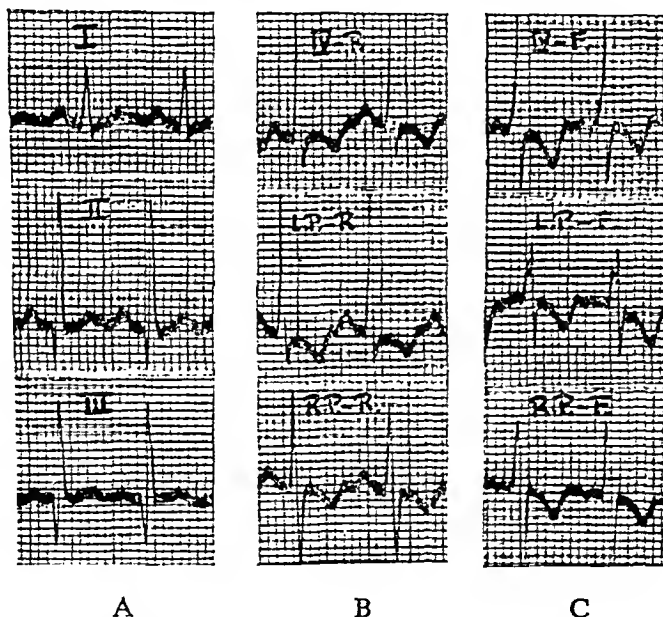


FIG. 4.—Electrocardiograms from a case of rheumatic pericarditis with effusion, showing normal limb leads (A), and inversion of the T wave in all chest leads whether paired with the right arm (B), or with the left leg (C).

It is concluded that in cases of pericarditis changes in the RS-T segment and in the T wave are well shown in chest leads; that these changes may last longer than the changes in limb leads, and that they may occur in association with normal limb leads. Chest leads may therefore be of value. Multiple leads may be useful to distinguish pericarditis from rheumatic carditis, for in the former the right pectoral lead may be normal, whereas in the latter if the T wave is inverted in the apical or in the left pectoral lead it will also be

inverted in the right pectoral lead. To distinguish pericarditis from anterior myocardial infarction attention should be paid to the QRS complex rather than to the T wave. For the distal electrode we prefer the right arm in children, but the left leg is equally suitable in adults.

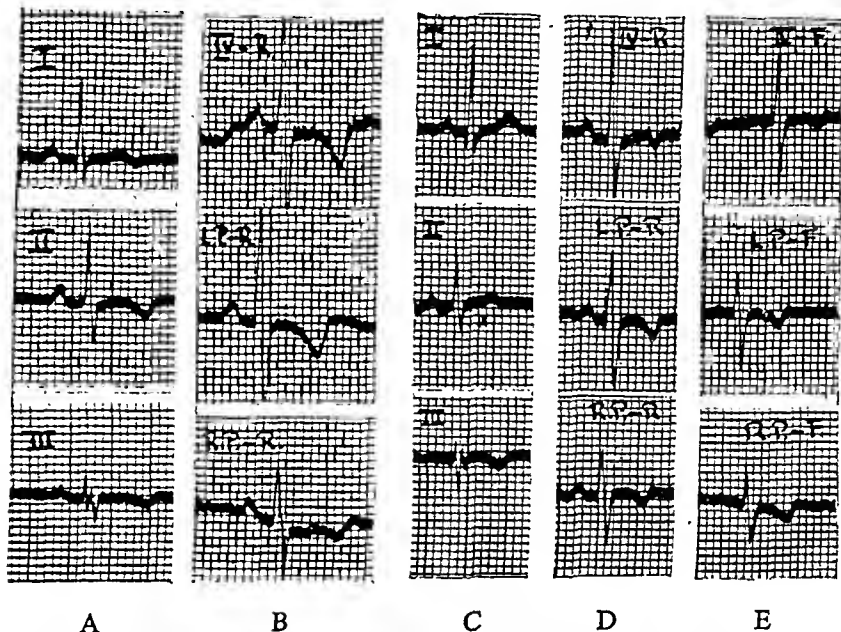


FIG. 5.—Electrocardiograms from a case of rheumatic pericarditis without effusion, showing how changes in chest leads may outlast those in limb leads.

- (A) Limb leads showing a typical T_2 pattern.
- (B) Chest leads paired with the right arm (same date).
- (C) Limb leads ten weeks later showing normal T waves.
- (D) Chest leads paired with the right arm (same date as C).
- (E) Chest leads paired with the left leg (same date as C).

LEFT VENTRICULAR ENLARGEMENT

There have been but few reports on the appearance of chest lead electrocardiograms in cases of left ventricular enlargement. Van Nieuwenhuizen and Hartog (1937b), using a left pectoral—left leg lead, found that there was a decrease in voltage of the R wave and an increase in voltage of the S wave in cases of hypertensive heart disease, so that R often measured less than 2 mm. and S more than 17 mm. In some cases they found absence of the R wave altogether. (To avoid confusion their terminology has been translated into the current one). Their left pectoral lead was taken from a fixed point on the chest wall close to the left border of the sternum, and was therefore very far to the right of the apex beat in cases with considerable left ventricular enlargement.

Hecht (1936), employing Wilson's neutral electrode (Wilson and others, 1934d), considered that inversion of the T wave in the apical lead in cases with

enlargement of the left ventricle indicated serious damage to the myocardium. His proximal electrode was placed in the anterior axillary line.

Roth (1937), using the old polarity, found reversal of the T wave in lead IV F, but not in the left pectoral—left leg lead, in some cases of hypertensive heart disease in which the apex beat was considerably displaced to the left. He concluded that lead IV F was simply lead III in such cases, and that the left pectoral lead was therefore the better chest lead. We find this argument a little difficult to follow. If the proximal electrode is placed over a heaving cardiac impulse in the anterior axillary line or thereabouts, the electrocardiogram so obtained cannot be very different from one obtained by a direct lead from the surface of the apex of the left ventricle (Wilson and others, 1932 b). Considering the position of the left ventricle in these cases it is likely that similar changes of potential will be found in the left arm, which because of its proximity will dominate the limb leads. In short, in such cases, lead III (and lead I) are almost semi-direct leads, the left arm acting almost as a proximal electrode. We fail to see that this detracts from the importance of lead IV, except that by examining the limb leads we might predict the appearance of lead IV.

Holzmann (1937), using an anterior-posterior lead and the new polarity, showed many examples of very small R waves and deep S waves in cases with considerable enlargement of the left ventricle. The T wave remained upright, for the proximal electrode was close to the sternum.

We have studied the chest lead electrocardiograms in 120 cases of left ventricular enlargement. The behaviour of the QRS complex was interesting. In the apical leads R was usually very tall, but in the left pectoral leads it often measured less than 2 mm. in height, and in the right pectoral leads it was even less conspicuous. In the right pectoral—right arm lead S was the dominant deflection in 97 per cent. of the cases compared with the 75 per cent. figure for normal controls. A monophasic downward deflection was rare in the left pectoral leads, occurring in two cases of syphilitic aortic incompetence and in one case of hypertensive heart disease, but in the right pectoral leads it occurred in three cases of syphilitic aortic incompetence and in four cases of hypertensive heart disease. There was no evidence of myocardial infarction in any of these cases.

Our findings with regard to the QRS complex are therefore in agreement with those of Van Nieuwenhuizen and Hartog (1937b), and with those of Holzmann (1937), and we conclude that very small R waves in the left or right pectoral leads cannot be accepted as evidence of myocardial infarction in cases with left ventricular enlargement, and that, in the presence of the latter, even monophasic downward deflections in the left pectoral lead must be interpreted with caution.

In studying the behaviour of the RS-T segment and of the T wave, we divided the cases into three groups according to the degree of enlargement of the left ventricle. This was always estimated radiologically by the same observer, P. W., throughout this work.

Group I consisted of fifty cases of slight left ventricular enlargement, most from hypertension, a few from aortic valvular disease. In some there was mild

to moderate breathlessness on exertion, and in others there were no cardiac symptoms. Limb leads showed left axis deviation with an upright T wave in lead I. Chest leads paired with the right arm yielded normal curves in every instance, wherever the proximal electrode. Chest leads paired with the left leg, however, showed a decrease in the incidence of an inverted T wave in the right pectoral lead from 58 per cent. in the controls to 14 per cent.

Group II consisted of fifteen cases with moderate left ventricular enlargement, mostly from hypertension. Effort was more limited by dyspnoea than in the previous group, but there was no orthopnoea or other evidence of left ventricular failure. Limb lead electrocardiograms showed left axis deviation with an upright T wave in lead I, some with and some without depression of the RS-T segment in that lead. In the former cases leads IV R and F showed a similar depression of the RS-T segment. Otherwise, and apart from the QRS changes previously mentioned, chest leads paired with the right arm were normal, but chest leads paired with the left leg showed an even lower incidence (one case only) of inversion of the T wave in the right pectoral lead than occurred in group I.

In group III there were fifty-five cases with considerable left ventricular enlargement, thirty-nine from hypertension, fifteen from aortic incompetence (mostly syphilitic), and one from aortic stenosis. Most had some evidence of left ventricular failure, and some had right ventricular failure also. Cases with angina pectoris or with a history of myocardial infarction were excluded. With limb leads there was inversion of the T wave in lead I only in thirty-three instances, in leads I and II but not in lead III in eleven instances, and in all three leads in five. In nearly all of these there was associated depression of the RS-T segment in the lead or leads in which the T wave was inverted. Depression of the RS-T segment in lead I without inversion of the T wave occurred in five of the remaining six cases, and a flat T wave in lead I was found in the sixth. Left axis deviation was always present except in those cases with inversion of the T wave in all leads.

With chest leads there was inversion of the T wave with associated depression of the RS-T segment in the apical leads alone in twenty-five instances, in both the apical and left pectoral leads but not in the right pectoral leads in three instances, and in all leads in two. When inversion of the T wave was confined to lead I in the limb leads, it was also confined to leads IV R and F in the chest leads; when it occurred in leads I and II, it was found in three out of eleven such cases in both the apical and left pectoral leads; and when it happened in all three limb leads it also happened in two out of five such cases in all three chest leads. These findings are illustrated in Fig. 6. When depression of the RS-T segment in lead I was the only change in limb leads, a similar depression of the RS-T segment was found in leads IV R and F but not in the other chest leads. The majority of cases in group III exhibited slight elevation of the RS-T segment in the pectoral leads, and it was this group especially which showed the small R waves and the large S waves previously described. Finally, it should be noted that of the fifty-five cases in this group only two showed inversion of the

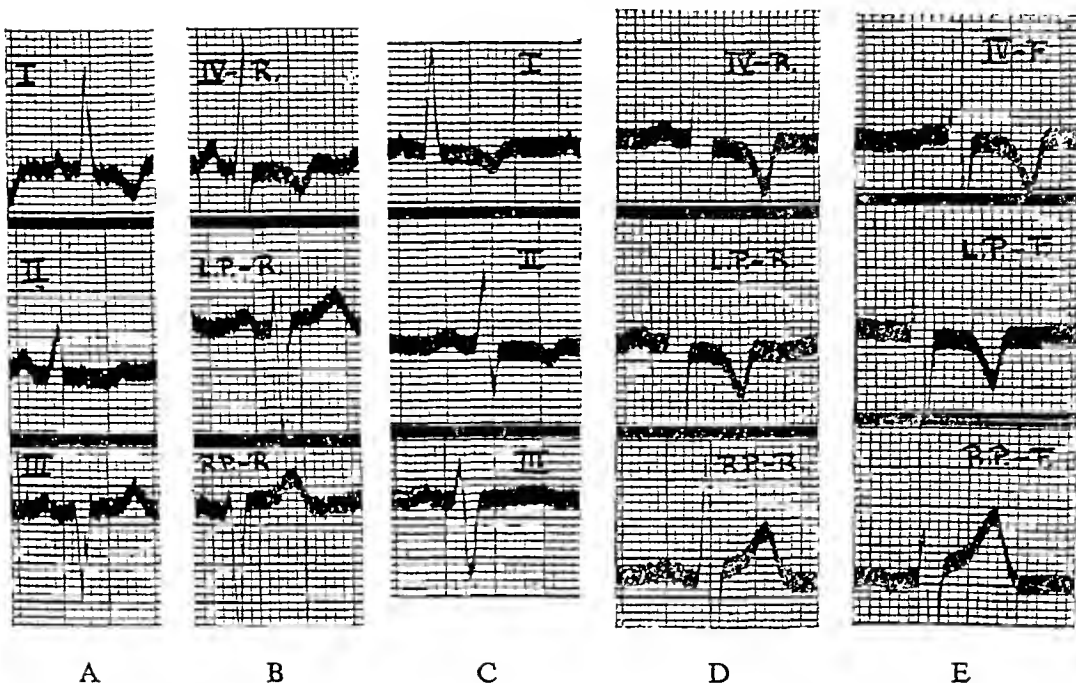


FIG. 6.—Electrocardiograms from two cases of hypertension with considerable enlargement of the left ventricle.

A and B. Limb leads (A), and chest leads paired with the right arm (B), in a case in which inversion of the T wave is confined to leads I and IV.

C, D and E. Limb leads (C), and chest leads paired with the right arm (D), and with the leg (E), in a case in which inversion of the T wave has extended to lead II and to the left pectoral leads in addition to leads I and IV.

T wave in the right pectoral—left leg lead, and in these two the T wave was inverted in every other lead including the three limb leads.

From a consideration of the facts which we have presented certain points arise which merit further attention.

First, the facts summarized in Table IV show that with progressive enlargement of the left ventricle the incidence of inversion of the T wave in the right pectoral—left leg lead fell from the normal figure of 58 per cent. to nil (excluding rare cases in which the T wave was inverted in all leads). In other words, if the left ventricle was significantly enlarged the T wave was upright in the right pectoral—left leg lead; if the T wave was inverted in this lead, the left ventricle was not significantly enlarged. We wondered whether displaced hearts due to a high diaphragm, which gave rise to left axis deviation in the standard leads, would produce an upright or an inverted T wave in this lead. To determine the answer to this question we studied normal pregnant women just before labour. We found twelve cases with left axis deviation in the limb leads. Of these, ten showed inversion of the T wave in the right pectoral—left leg lead, and two showed a diphasic T wave. In addition the T wave was inverted in four instances in the left pectoral—left leg lead, and in two instances in lead IV F. We conclude that in the right pectoral—left leg lead we have a means of distin-

TABLE IV
LEFT VENTRICULAR ENLARGEMENT

INVERSION OF THE T WAVE IN THE RIGHT PECTORAL—LEFT LEG LEAD

	No. of cases	Percentage with inverted T wave
NORMAL ADULTS	50	58 %
LEFT VENTRICLE +	50	14 %
LEFT VENTRICLE ++	15	7 %
LEFT VENTRICLE +++	55	0 %*

* Excluding two cases with inverted T waves in all leads

guishing enlargement of the left ventricle from displacement of the heart due to a high diaphragm. If the T wave is upright no inference can be drawn, but if it is inverted significant enlargement of the left ventricle is unlikely. We have found this rule of value in attempting to assess the size of the left ventricle in cases of obesity. When the proximal electrode is paired with the right arm the results are far less helpful because the T wave is very rarely inverted in this lead. Electrocardiograms showing the absence of significant left ventricular enlargement in a case of obesity with hypertension are illustrated in Fig. 7.

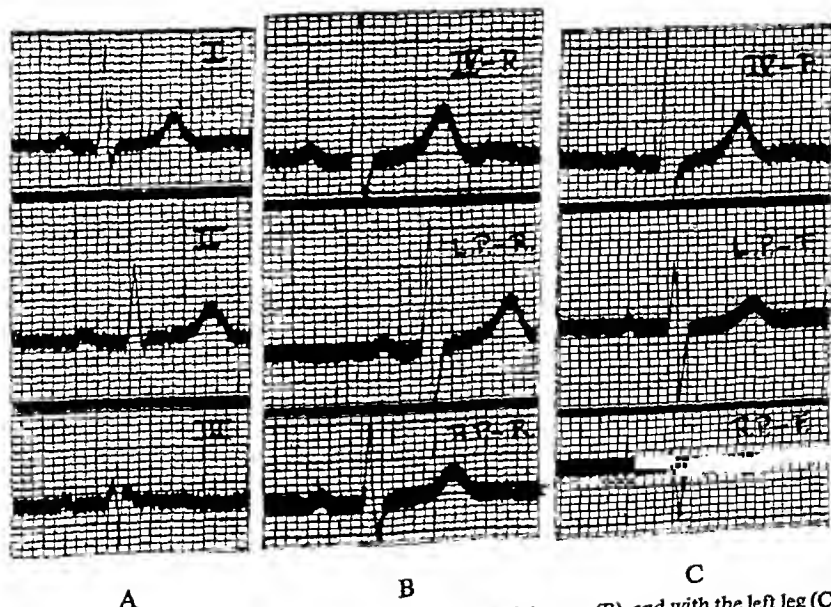


FIG. 7.—Limb leads (A), and chest leads paired with the right arm (B), and with the left leg (C), in a case of obesity. Note the inverted T wave in the right pectoral—left leg lead.

Secondly, the point arises as to why the T wave should be inverted in lead IV in only eighteen out of thirty-three cases of considerable left ventricular enlargement in which it was inverted in lead I. On re-examining these records we found that when the T wave was inverted in lead IV the R deflection dominated the QRS complex, whereas when the T wave was upright the S deflection dominated. This was clear evidence that the proximal electrode had been placed within the apex beat in these latter cases, so that the leads were more left pectoral than apical. We have since re-investigated a few of these patients and have found that great care had to be taken in placing the proximal electrode, but that when this was placed truly upon the apex beat the T wave became inverted and the R deflection dominated the QRS complex as expected.

Thirdly, the facts show that in cases of left ventricular enlargement if the T wave is inverted in any chest lead, it is also inverted (and usually more so) in leads in which the proximal electrode is shifted to the left. This is the reverse of what happens in normal children and in cases of rheumatic carditis, and, as will be shown subsequently, in cases of right ventricular enlargement.

Fourthly, it is evident that depression of the RS-T segment and inversion of the T wave in lead IV R or F do not indicate myocardial infarction in the presence of sufficient enlargement of the left ventricle.

Summary of the effects of left ventricular enlargement on the chest lead electrocardiogram

1. Though the R deflection is often exceedingly tall in leads IV R and F, there is an increased incidence of small R waves and deep S waves in the pectoral leads.

2. With progressive enlargement of the left ventricle the incidence of inversion of the T wave in the right pectoral—left leg lead falls steadily from 58 per cent. in the controls to nil in the cases with considerable enlargement. Patients with cardiac displacement due to a high diaphragm usually exhibit an inverted T wave in this lead.

3. In the lesser degrees of left ventricular enlargement the RS-T segment and the T wave are normal in the apical and left pectoral leads.

4. In the greater degrees of left ventricular enlargement the RS-T segment is depressed and the T wave is inverted in leads IV R and F, and occasionally in the left pectoral leads.

RIGHT VENTRICULAR ENLARGEMENT

Groedel (1934) maintains that deformities in the QRS complex and inversion of the T wave in right ventricular semi-direct leads indicate disease of the right ventricle. Hecht (1936), using Wilson's neutral distal electrode, found that right ventricular enlargement caused inversion of the T wave in the right pectoral lead, and sometimes a large Q wave.

To determine the effect of right ventricular enlargement upon the chest

lead curves we investigated thirty-five cases of mitral stenosis, six of chronic cor pulmonale, five of acute cor pulmonale following pulmonary embolism, and four of congenital pulmonary stenosis, making a total of fifty cases with right ventricular enlargement or stress. Patients with aortic valvular disease or with hypertension in addition were excluded.

The QRS complex was usually normal in the apical and in the left pectoral leads, but in the right pectoral leads the main QRS deflection was upright in about a third of the cases, rather more than a third when the proximal electrode was paired with the right arm, and rather less than a third when it was paired with the left leg. Pronounced notching of the R wave was sometimes observed associated with delay in the onset of the intrinsic downward deflection, and occasionally there was prominent Q wave, both these abnormalities being confined to the right pectoral leads. These features are illustrated in Fig. 8.

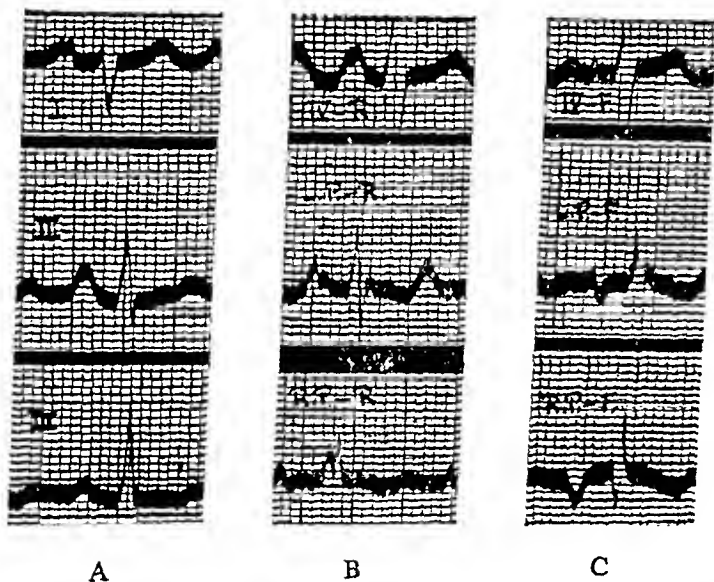


FIG. 8.—Limb leads (A), and chest leads paired with the right arm (B), and with the left leg (C), in a case of mitral stenosis with enlargement of the right ventricle. Note the absence of S waves and the inverted T waves in the right pectoral leads, and the Q wave in the right pectoral—left leg lead.

The frequency of inversion of the T wave in leads paired with the left leg is shown in Table V. (The incidence was somewhat lower in leads paired with the right arm.) It was found in 20 per cent. in lead IV, in 35 per cent. in the left pectoral lead, and in 75 per cent. in the right pectoral lead. As in normal children and as in cases of rheumatic carditis, if the T wave was inverted in any lead it was also inverted, and usually more so, when the proximal electrode was shifted to the right. In table V the incidence of inversion of the T wave in right ventricular enlargement is compared with that in normal adults, in normal children and in rheumatic carditis. This comparison suggests that the cause of inversion of the T wave in normal children and in rheumatic carditis is relative

TABLE V
RIGHT VENTRICULAR ENLARGEMENT

INVERSION of the T WAVE in LEFT LEG paired LEADS

	LEAD		
	TV-F	L.P.-F	R.P.-F
NORMAL ADULTS	0 %	2 %	58 %
NORMAL CHILDREN	0 %	21 %	65 %
RHEUMATIC CARDITIS	16.6 %	33.3 %	66.6 %
R.V. ENLARGEMENT	20 %	35 %	75 %

right ventricular dominance, and this finds support in the fact that increased left ventricular dominance has an opposite effect upon the T wave. It will be remembered that when the left ventricle is considerably enlarged the T wave is never inverted in the right pectoral—left leg lead (except in rare cases in which T is inverted in all leads including the three limb leads). With moderate left ventricular enlargement the T wave is inverted in 7 per cent. in this lead ; with slight left ventricular enlargement it is inverted in 14 per cent. ; in normal adults in 58 per cent. ; in normal children in 65 per cent. ; in cases of rheumatic carditis in 66.6 per cent. ; and finally in cases of right ventricular enlargement in 75 per cent. We have expressed these facts altogether in Table VI. This shows clearly the influence of right ventricular enlargement upon the direction of the T wave in the chest lead electrocardiograms employed.

TABLE VI
THE INFLUENCE OF VENTRICULAR ENLARGEMENT
UPON THE DIRECTION OF THE T WAVE

Percentage of cases with inversion of the T wave

	Lead TV-F	Lead L.P.-F	Lead R.P.-F.
L.V. ENLARGEMENT +++	58	9	4
L.V. ENLARGEMENT ++	0	0	7
L.V. ENLARGEMENT +	0	0	14
NORMAL ADULTS	0	2	58
NORMAL CHILDREN	0	21	65
RHEUMATIC CARDITIS	16.6	33.3	66.6
R.V. ENLARGEMENT	20	35	75

In general, the extent of T wave inversion was parallel to the degree of right ventricular enlargement, and when the T wave was inverted in lead IV the right ventricle was usually considerably enlarged. Illustrations of inverted T waves in cases of right ventricular enlargement are shown in Fig. 9.

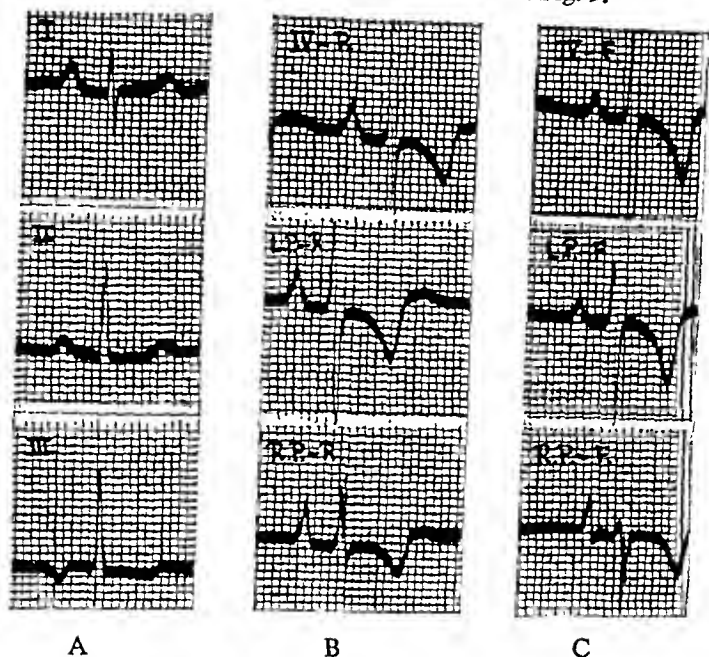


FIG. 9.—From a case of mitral stenosis with considerable enlargement of the right ventricle.

(A) Limb leads.

(B) Chest leads paired with the right arm.

(C) Chest leads paired with the left leg.

Note inversion of the T wave in all chest leads (the tall spiked P wave in the right pectoral leads probably indicates right auricular hypertrophy).

Special attention must be paid to the cases of acute cor pulmonale following pulmonary embolism. In these, inversion of the T wave was transient, and was most marked and lasted longest in the right pectoral leads. The sequence of events was remarkably similar in all five cases. The first record, obtained within twenty-four hours from the onset, showed inversion of the T wave in both pectoral leads and sometimes in the apical leads as well; the first change occurred two or three days later when the T wave in lead IV became upright if it had been previously inverted; the second change, after a few more days, occurred when the T wave became upright in the left pectoral lead; and finally, the T wave became upright in the right pectoral lead. The usual sequence of events is illustrated in Fig. 10.

These findings are important for two reasons: first, because they suggest that inversion of the T wave of the type described may occur from right ventricular stress quite apart from hypertrophy; and secondly, because they may be of great help in the differential diagnosis of pulmonary embolism from posterior myocardial infarction.

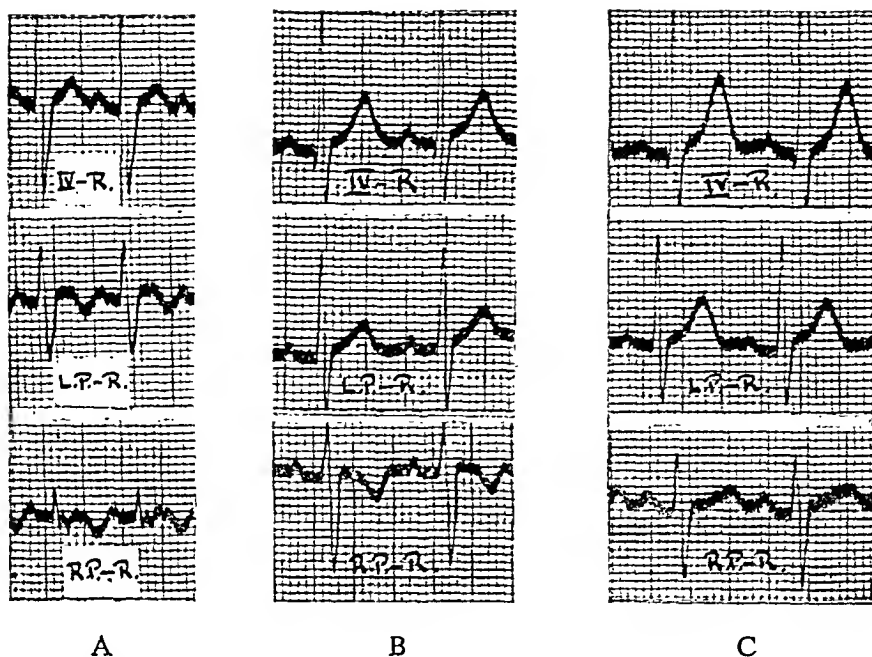


FIG. 10.—Serial chest lead electrocardiograms paired with the right arm from a case of acute cor pulmonale following pulmonary embolism.

- (A) Within twenty-four hours of the onset, showing inversion of the T wave in the left and right pectoral leads.
- (B) A week later, showing inversion of the T wave in the right pectoral lead only.
- (C) Eighteen days after the onset, showing upright T waves in all leads.

Summary of the effects of right ventricular enlargement upon the chest lead electrocardiogram

1. The main QRS deflection is upright in the right pectoral leads in about a third of the cases. Such curves are especially significant when the proximal electrode is paired with the left leg.

2. Marked notching of the R wave associated with a late intrinsic downward deflection may sometimes occur in the right pectoral lead, and occasionally there may be a prominent Q wave.

3. Inversion of the T wave is common and obeys the rule which may be applied to normal children and to cases of rheumatic carditis, i.e. if the T wave is inverted in any lead, it is also inverted (and usually more so) in leads in which the proximal electrode is shifted to the right.

4. Transient T wave changes of the same type are seen in cases of acute cor pulmonale following pulmonary embolism, and may be of considerable help in diagnosing the condition from posterior basal myocardial infarction.

5. The incidence of inversion of the T wave is greater when the proximal electrode is paired with the left leg; but its significance is greater when the proximal electrode is paired with the right arm.

These findings are in contrast to those of left ventricular enlargement.

BUNDLE BRANCH BLOCK

The form of the chest lead electrocardiogram in cases of bundle branch block in human beings was originally worked out by Wilson, Macleod and Barker (1932 b), their publication appearing one month after the original article by Wolferth and Wood (1932 a) recommending the use of chest leads as an aid in the diagnosis of myocardial infarction. Wilson, Macleod and Barker (1932 b) used multiple chest leads paired with the left leg, and these would now be called leads CF 1, 2, 3 and 4 (*Standardization of Präcordial Leads*, 1938). The object of their paper was to show that what was then called right bundle branch block was in reality left bundle branch block and vice versa. Using the old polarity they determined that "when bundle branch block is present the chief upstroke of the ventricular complex in semi-direct leads is early when the exploring electrode is placed close to the ventral surface of the contralateral ventricle and late when this electrode is placed close to the surface of the homolateral ventricle. In the former case the fibre usually remains above, in the latter case it usually remains below the base line throughout the greater part of the QRS interval." They also stated that the right ventricle was favourably situated for semi-direct leads from its ventral surface, but that the left ventricle was not so favourably situated.

Wilson, Johnston, Hill, Macleod and Barker (1934 c), using similar multiple leads but paired with a neutral indifferent electrode, showed that an abnormally long QRS interval and a broad S deflection in lead I signified right bundle branch block. Chest leads V₁, V₂ and V₃ exhibited a late chief upstroke (old polarity) and leads V₄ and V₅ an early one.

In certain cases of septal infarction with bundle branch block, Wilson, Hill and Johnston (1934 a) advise the use of chest leads for proper interpretation. They described the production of right bundle branch block of the type just mentioned by experimental infarction of the interventricular septum in three dogs. Wilson, Johnston and Barker (1934 b) also advise the use of chest leads in order to interpret limb lead electrocardiograms which exhibit a bizarre form of bundle branch block. In three such cases the limb lead electrocardiograms were illustrated and were thought to be suggestive of left rather than right bundle branch block, but chest leads showed clearly that they signified right bundle branch block.

Our series includes twenty cases of bundle branch block, ten left and ten right. We found that the appearances in the left and right pectoral leads were consistent in all cases. In left bundle branch block (new terminology) the main QRS deflection was downwards with an early intrinsic downward deflection, followed by a large upright T wave; in right bundle branch block of the type described by Wilson and his associates (1934 c), and by Evans and Turnbull (1937) in this country, the main QRS deflection was upwards with a late intrinsic downward deflection and the T wave was inverted. The appearances in the apical leads were less consistent, no doubt depending upon whether the proximal electrode represented a left or a right ventricular or a septal contact. Thus in left bundle branch block seven cases presented similar features to those in the

pectoral leads, and only three showed a late intrinsic downward deflection with an upright QRS complex and inversion of the T wave. In right bundle branch block the intrinsic downward deflection was early in lead IV in seven cases, followed by a broad sluggardly S deflection and an upright T wave, but in the other three cases the appearances were similar to those in the pectoral leads (see Figs. 11 and 12).

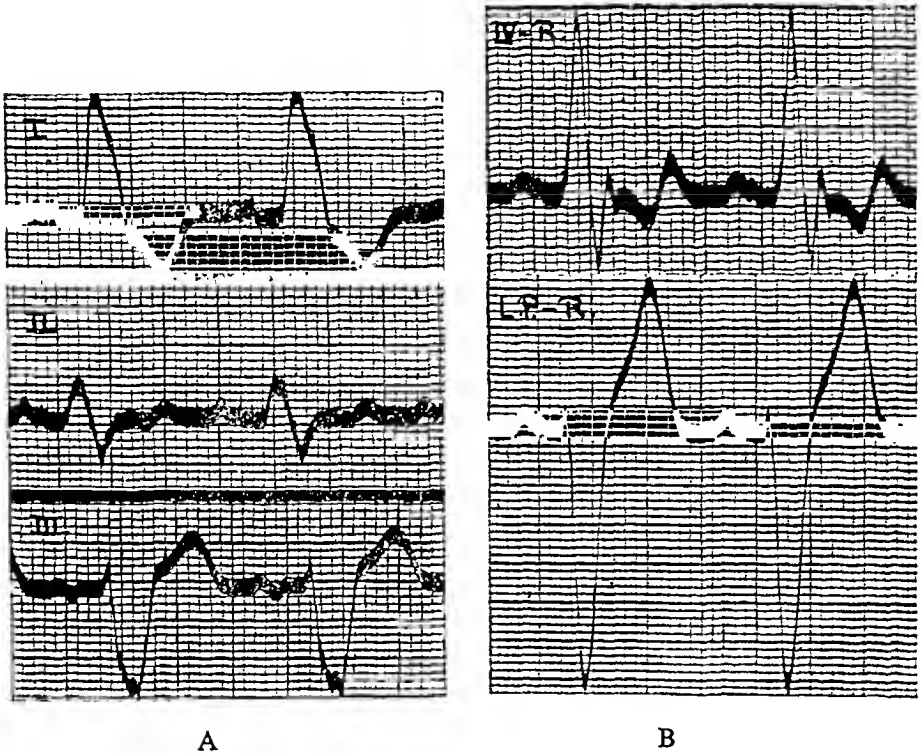


FIG. 11.—Left bundle branch block (new terminology).

(A) Limb leads.

(B) Chest leads paired with the right arm.

Above : lead IV R showing a somewhat delayed intrinsic downward deflection and a diphasic T wave.

Below : the left pectoral lead (the right pectoral lead was similar) showing an early intrinsic downward deflection, a very deep S wave, and a very tall T wave.

It is, therefore, clear that for clinical work the pectoral leads are more valuable than lead IV for interpreting doubtful or bizarre forms of bundle branch block, and that the choice of distal electrode is a matter of indifference. It should be noted that when there is difficulty in distinguishing left bundle branch block from left axis deviation with inversion of T, no help can be obtained from chest leads ; but that when there is difficulty in distinguishing right bundle branch block from right axis deviation with inversion of T3, the left pectoral lead usually makes correct interpretation easy. Reference to the findings in cases of considerable left and right ventricular enlargement will clarify these remarks.

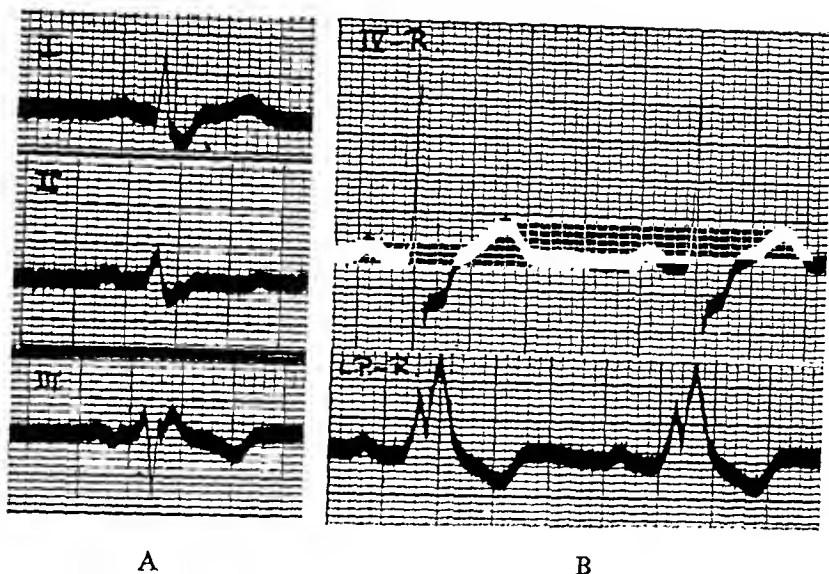


FIG. 12.—Right bundle branch block—common type (new terminology).

(A) Limb leads.

(B) Chest leads paired with the right arm.

Above : lead IV R showing a normally timed intrinsic downward deflection and gross slurring of S. The appearances are similar to those in lead I.

Below : the left pectoral lead (the right pectoral lead was similar) showing a notched upright QRS complex with a late intrinsic downward deflection, and an inverted T wave.

DIGITALIS

The effect of digitalis upon the limb lead electrocardiogram is well known. There is a characteristic depression of the RS-T segment. Strauss and Katz (1935) using chest leads came to the conclusion that either elevation or depression of the RS-T segment might occur. They used the old polarity. Their illustrations of elevation of the RS-T segment were convincing, but the same cannot be said of their example of depression of that segment.

Stewart and Watson (1938) have also investigated the effect of digitalis upon the chest lead electrocardiogram. Using an anterior-posterior lead and the old polarity they found that elevation of the RS-T segment occurred in the majority of cases, but that occasionally there were other effects. The electrocardiograms showing these other effects, which included depression of the RS-T segment, were bizarre.

Holzmann (1937), using an anterior-posterior chest lead and the new polarity, found that digitalis commonly caused depression of the RS-T segment similar in character to that seen in limb lead electrocardiograms. Occasionally, however, especially when there was eccentric hypertrophy of the left ventricle or of both ventricles, digitalis produced a dome shaped RS-T segment which was elevated to a maximum of 0.2 mv. above the iso-potential level. These curves resembled those of myocardial infarction, and correct interpretation

was sometimes difficult. When elevation exceeded 0.2 mv., a digitalis effect could be excluded.

We have used chest leads in fifteen cases treated with digitalis. Depression of the RS-T segment, similar in character to that seen with limb leads, and often in an exaggerated form, was found in every instance. It was most pronounced in lead IV except in those cases with marked right ventricular dominance when it was most evident in the right pectoral lead (see Fig. 13). It was shown rather

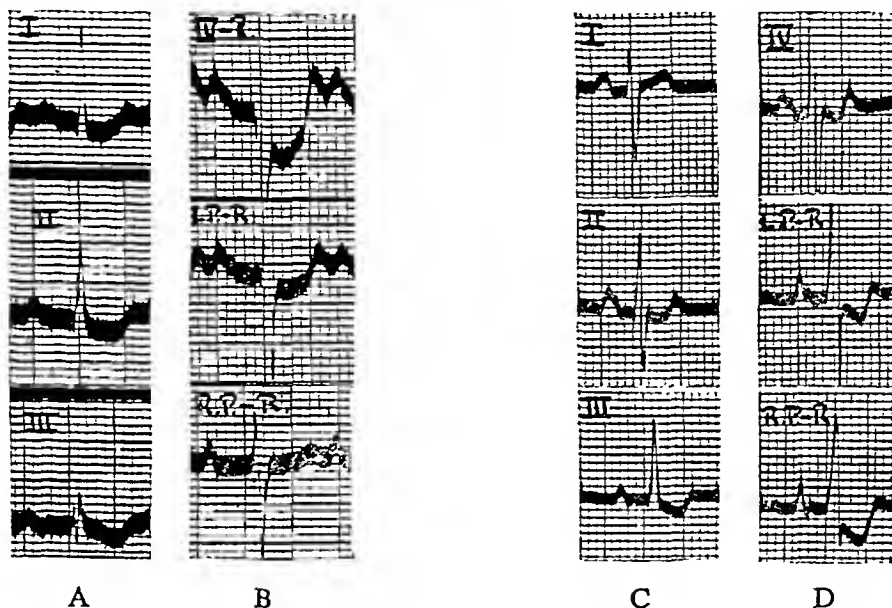


FIG. 13.—Limb leads (A), and chest leads paired with the right arm (B), in a case of digitalis intoxication. There is very marked depression of the RS-T segment in lead IV, but none in the right pectoral lead. Case of thyrotoxicosis.

(C), (D) Limb leads, and chest leads paired with the right arm, in a case of marked right ventricular dominance due to mitral stenosis, pulmonary hypertension and probable pulmonary embolism. The digitalis effect is most marked in the right pectoral lead.

better when the proximal electrode was paired with the right arm than when it was paired with the left leg.

It is concluded that lead IV R is suitable for showing the effect of digitalis except in cases with marked right ventricular dominance when the right pectoral lead should be used, and that when there is doubt as to the proper interpretation of a possible digitalis effect with limb leads, chest leads may be helpful by showing this effect in an exaggerated form.

MYOCARDIAL INFARCTION

Wood and Wolferth (1932, 1933) showed that an anterior-posterior chest lead electrocardiogram would produce typical changes in the RS-T segment after experimental ligation of the anterior descending branch of the left coronary artery of the dog, when the limb lead electrocardiogram was normal. They concluded that this might also apply to certain cases of myocardial infarction in

man. An opportunity to test this suggestion soon presented itself. A case, clinically diagnosed as myocardial infarction, failed to show changes with the limb leads. An anterior-posterior chest lead was employed, and the electrocardiogram so obtained showed a remarkable deviation of the RS-T segment from the iso-potential level. This case subsequently exhibited diagnostic changes in the limb leads. To it was added another case which showed typical RS-T changes in both limb and chest leads, and then with thirty-three controls the facts were published (Wolferth and Wood, 1932 a) prior to the experimental reports given above. Shortly afterwards they published a short article (1932 b) describing three cases of myocardial infarction in which the changes were more evident in limb than in chest leads. One of these cases exhibited a typical T1 type of coronary curve, but the other two were probably both posterior infarctions.

Several hasty reports by other authors followed and have been sharply criticized by Roth (1935). But in the last six years certain facts have become established. In anterior myocardial infarction changes occur in the QRS complex, in the RS-T segment and in the T wave, and any one of these changes may be shown only or best in one particular lead either limb or præcordial. Wilson and his associates have made a special study of the behaviour of the QRS complex with limb (Wilson and others, 1932 a, 1933) and with semi-direct leads (Johnston and others, 1935; Wilson and others, 1932 a, 1935 a, 1935 b, 1933), both in the dog and in man. They have shown experimentally that monophasic downward deflections (new polarity) are obtained from areas underlying which there is infarction of the whole thickness of the ventricular wall, but that at the edges of the infarct where there is living tissue, or over the centre of the infarct if it only involves part of the thickness of the ventricular wall, a W complex is usual. Semi-direct leads taken from points overlying healthy muscle away from the infarct yield normal QRS complexes. These QRS changes may be transient or permanent according to the degree of recovery of the muscle deprived of its blood supply. In clinical cases they found that QRS changes were more likely to be permanent than T wave changes.

The occurrence of a monophasic downward deflection in the chest lead in cases of anterior myocardial infarction has been well established (Bohning and Katz, 1938; Donzelot and Pelaez, 1938; Faulkner, 1936; Feinstein and Lieberman, 1937; Freeman, 1937; Goldbloom, 1934; Holzmans, 1937; Jervell, 1935; Master and other, 1937; Wood and others, 1933), but little attention has been paid to the W complex. Amongst the authors who stress the importance of a monophasic downward deflection are Master, Dack, Kalter and Jaffe (1937) who also state that a very small R wave is significant. They found it in 37 per cent. of cases with ischæmic heart disease compared with the figure of 7.5 per cent. for normal controls. When one considers that about 30 per cent. of cases with ischæmic heart disease have considerable enlargement of the left ventricle from hypertension or from syphilitic aortic incompetence, it is seen that the figure of 37 per cent. is exactly what one would predict, for we have already shown that cases with considerable enlargement of the left ventricle

ordinarily have a very small R wave in the left pectoral lead which is more or less the lead they used.

We have analysed the QRS complex in eighteen cases of anterior myocardial infarction. In lead IV R or F we found a W complex in no less than twelve cases, and a monophasic downward deflection in only three. The shape of the W varied considerably, but so long as there were three conspicuous deflections, Q, R and S, we included it. In the left and right pectoral leads QRS was represented by a monophasic downward deflection in fifteen cases. Eight patients were followed for periods of six months to two and a half years : the W complex was permanent in three and transient in two ; the monophasic downward deflection was permanent in five and transient in two.

The finding of W complexes in apical leads and monophasic downward deflections in the pectoral leads, which have also been recorded by Kossmann and de la Chapelle (1938), is a little difficult to understand. According to the experimental work of Wilson and his associates already mentioned, monophasic downward deflections might be expected in lead IV over the site of the infarct, and W complexes in the left pectoral lead at the edge of the infarct, in the common cases of anterior apical myocardial infarction. If the infarct should involve only the inner part of the muscle wall, the W complex would be understood at the apex, but in that case why should there be a monophasic downward deflection in the left pectoral lead ?

Elevation of the RS-T segment is commonly seen in the early stages of anterior myocardial infarction, and has frequently been described (Bohning and Katz, 1938 ; Donzelot and Pelaez, 1938 ; Feinstein and Lieberman, 1937 ; Freeman, 1937 ; Holzmänn, 1937 ; Jervell, 1935 ; Lieberman and Liberson, 1933 ; Swan, 1937 ; Van Nieuwenhuizen and Hartog, 1937 a ; Willcox and Lovibond, 1937 ; Wilson, 1936) since the article by Wolferth and Wood (1932). In our series elevation of the RS-T segment occurred in nine out of twelve cases which were investigated sufficiently early. It was always evident in lead IV and in the left pectoral leads, but it only occurred in the right pectoral lead in four cases. The choice of distal electrode was a matter of indifference. As with limb leads this change was always transient.

Subsequent inversion of the T wave has been described by practically all authors on the subject of chest leads in myocardial infarction, and Wolferth and Wood (1933) have reported seven cases in which these T waves were " huge." All our cases showed subsequent inversion of the T wave in the apical leads, and all but three in the left pectoral leads. In the right pectoral—right arm lead the T wave was inverted in five cases, and in the right pectoral—left leg lead in seven. Of eight cases followed for a sufficient period of time the inversion of the T wave was permanent in four cases in the apical leads, in three cases in the left pectoral leads, and in four cases it was transient.

Characteristic curves showing the W complex, the monophasic downward deflection, the elevation of the RS-T segment, and the inverted T wave are shown in Fig. 14.

There have been different reports concerning the findings with chest leads in cases of posterior myocardial infarction. All are agreed that the QRS

complex is not affected, and that the T wave is not inverted. Though some (Jervell, 1935 ; Swan, 1937 ; Wood and others, 1933) have concluded that the RS-T segment is usually unaffected, others have shown that there may be marked depression of this segment in the early stage of posterior infarction (Bohning

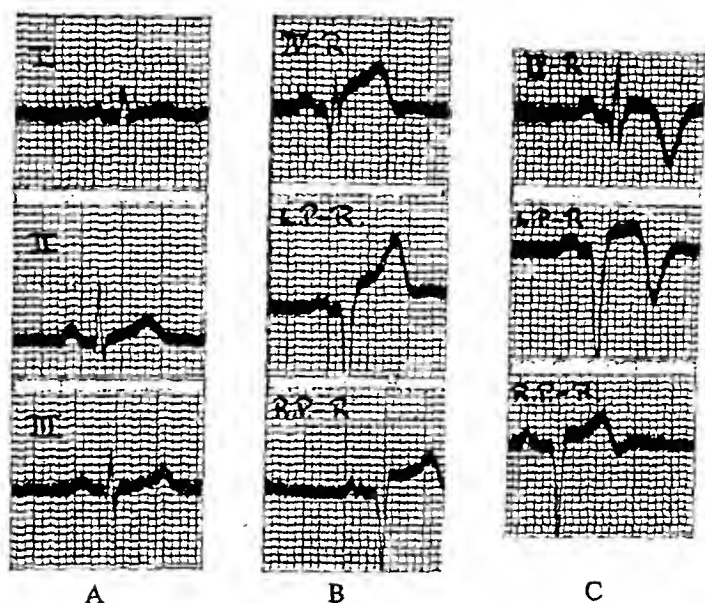


FIG. 14.—From a case of anterior myocardial infarction.

Limb leads (A), and chest leads paired with the right arm (B), showing a deformed W complex in lead IV, monophasic downward deflections in the pectoral leads, and elevation of the RS-T segment in all chest leads.

Chest leads paired with the left arm (C), a week later, showing a typical W complex in lead IV, monophasic downward deflections in the pectoral leads, somewhat less elevation of the RS-T segment in all chest leads, and sharp inversion of the T wave in lead IV and in the left pectoral lead.

and Katz, 1938 ; Feinstein and Lieberman, 1937 ; Holzmann, 1937 ; Willcox and Lovibond, 1937 ; Wilson and others, 1932 a). It has also been shown that as the RS-T segment approaches or resumes the iso-potential level, the T wave may become very tall (Bohning and Katz, 1938 ; Feinstein and Lieberman, 1937 ; Willcox and Lovibond, 1937 ; Wilson and others, 1932 a).

Fifteen cases of posterior myocardial infarction were included in our series. QRS was normal in all instances. The RS-T segment was depressed in the apical leads in eight out of ten cases which were investigated sufficiently early. This depression was not so evident in the left pectoral leads and did not occur at all in the right pectoral leads. Inversion of the T wave did not occur, but in three instances an upright T wave of very high voltage succeeded the early depression of the RS-T segment. The distal electrode did not materially influence any of these findings (see Fig. 15).

The characteristic electrocardiographic changes of anterior myocardial infarction are very rarely restricted to chest leads if serial records are obtained,

but they may occur earlier in chest leads, where they may be diagnostic when still of doubtful significance in limb leads, and they may last longer in chest leads. Very occasionally an infarct may affect lead I and not the chest leads.

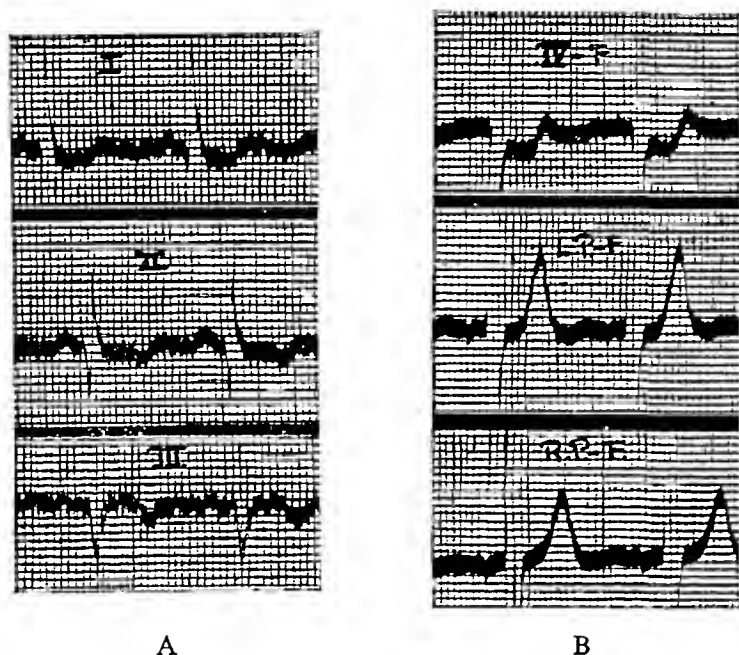


FIG. 15.—From a case of posterior myocardial infarction.

(A) Limb leads.

(B) Chest leads paired with the left leg, showing depression of the RS-T segment in lead IV, and tall T waves in the pectoral leads.

Wolferth and Wood (1932 b) reported such a case, and we have recently seen an example.

In our series of thirty-three cases of myocardial infarction serial limb leads were diagnostic of the condition in all but one instance, but in four others the changes occurred earlier in the chest lead graphs so that a correct diagnosis was made sooner. We derived no help from the chest leads in the cases of posterior myocardial infarction, for in these the limb leads required no support, and the chest leads had but little to give.

Before concluding, reference must be made to the value of chest leads in cases of multiple infarction. Wolferth and Wood (1935), and Feinstein and Lieberman (1937) have drawn attention to this.

A combination of anterior and posterior myocardial infarction may give rise to an atypical limb lead electrocardiogram which causes difficulty in diagnosis. In this event, chest leads may prove of use by unmasking the anterior infarct. The atypical electrocardiograms of the two cases, which came to autopsy in the paper by Wolferth and Wood (1935) were examples of the T_2 pattern described by Wood (1937) in cases of pericarditis and hæmopericardium, and it is therefore unfortunate that no statement was made as to the

presence or absence of pericarditis in the two cases mentioned. However, there can be little doubt as to the truth of their contention, and we have recently seen a good example in which limb leads were atypical but suggested posterior myocardial infarction, whereas chest leads were diagnostic of anterior infarction. Autopsy showed a large infarct at the apex of the left ventricle anteriorly, but spreading round to involve a considerable portion of the posterior wall.

*Summary of the Effects of Myocardial Infarction on the Chest Lead
Electrocardiogram*

A. In anterior myocardial infarction

1. QRS is often represented by a W complex in the apical leads, and by a monophasic downward deflection in the pectoral leads.
2. Initial elevation of the RS-T segment and subsequent inversion of the T wave commonly occur in both apical and left pectoral leads but are less evident in the right pectoral leads.
3. Any one of these changes, except elevation of the RS-T segment which is always transient, may or may not be permanent.
4. Both the right arm and the left leg are entirely satisfactory distal electrodes for the demonstration of these changes.

B. In posterior myocardial infarction

1. The QRS complex is normal.
2. Initial depression of the RS-T segment is common, and is most evident in the apical leads.
3. Very tall upright T waves are sometimes seen in the later stage either in the apical or in the left pectoral leads or in both.

For clinical work, chest leads are of undoubted value in cases of suspected myocardial infarction, especially by enabling one to make an earlier diagnosis in acute cases, and a correct diagnosis in cases seen for the first time some months after the event.

ANGINA PECTORIS

Chest leads have been considered helpful in the diagnosis of angina pectoris. Thus H. D. and S. A. Levine (1936), using a left para-sternal—left leg lead in addition to lead IV F, found that 16 per cent. of their cases of angina pectoris lacked an R wave. In another series of forty-four autopsy cases they showed that an absent R wave in lead IV F was associated with myocardial infarction in twelve out of fifteen cases. Two of the other three had bundle branch block, and the third had tuberculous pericarditis. (To avoid confusion we have translated their nomenclature into the current terminology.) They concluded that an absent R wave in the leads they used was important evidence of ischaemic heart disease.

Willcox and Lovibond (1937), preferred a left para-sternal—right arm lead. They investigated sixty-two cases of angina pectoris. In thirty-four the

electrocardiogram was normal ; in eleven both limb and chest leads were abnormal ; in nine the limb leads were abnormal, but the chest lead was normal ; and in eight the limb leads were normal, but the chest lead abnormal. The abnormalities in the chest leads consisted of very small or absent R waves and inversion of the T waves.

Edeiken, Wolferth and Wood (1936) considered that reversal of the T wave in their antero-posterior chest lead should be considered pathological when it was the only abnormality of the adult electrocardiogram. In such cases they suspected coronary artery disease.

The chest lead electrocardiograms in cases of angina pectoris must be interpreted with caution. For if there is associated hypertensive heart disease or aortic valvular disease with much enlargement of the left ventricle, an inverted T wave in the apical leads and a very small R wave in the pectoral leads are only to be expected, and cannot be used to support the diagnosis of angina pectoris. There were twenty-seven cases of angina pectoris in our series. Only three of these showed chest lead abnormalities which could not be accounted for by the known underlying condition, and in these three there was inversion of the T wave in leads IV R and F but not in the pectoral leads. The limb leads of these three cases were normal.

It is concluded that chest leads may be of service in giving support to the diagnosis of angina pectoris by revealing the presence of previous myocardial infarction. Both lead IV and the left pectoral leads are therefore advised, the former to show W complexes, the latter monophasic downward deflections, and either or both, inverted T waves.

DISCUSSION

THE DISTAL ELECTRODE

The choice of distal electrode lies between the dorsal electrode originally used by Wolferth and Wood (1932 a), the neutral electrode devised by Wilson and his associates (1934 d), and one of the limb electrodes. Because the dorsal electrode is inconvenient to apply, and because it has not been shown to have any advantage over the others, it seems wise to discard it. We have had no experience of Wilson's neutral electrode, but because it requires additional apparatus it is unlikely to meet with much favour in clinical work unless it proves to have definite advantages, and so far there is little evidence of this. Keller (1937), after comparing the neutral electrode with the right arm electrode used by Groedel (1934), came to the conclusion that the latter was preferable both on theoretical and practical grounds. The majority of workers now use one of the limb electrodes, and the most favoured are the left leg and the right arm. The left leg has been more widely used for two reasons : first, because the technique was simpler with the old polarity, and secondly because more work had been done with this electrode on normal controls. Neither of these reasons is now valid. With the new polarity the technique is simpler with the right arm electrode, and adequate work has now been done with this electrode

on normal controls. The choice between these two electrodes should be made on their respective merits.

If only one chest lead is used, lead IV (the apical lead) has been recommended by the Cardiac Society of Great Britain and Ireland and by the American Heart Association. Now in lead IV, there is only one difference between the distal electrodes under consideration: in young children lead IV F may occasionally show a diphasic T wave (Sorsky and Wood, 1937), and if the proximal electrode is placed slightly inside the apex beat the T wave may be inverted, whereas lead IV R exhibits an upright T wave in normal controls of any age, and the proximal electrode may be placed well inside the apex beat without altering the direction of the T wave. Since lead IV R is the simpler lead with the new polarity, it has two advantages and no disadvantages, and we, therefore, recommend it without hesitation.

If multiple chest leads are used the problem becomes more complicated. The left leg has the advantage when chest leads are used to distinguish left ventricular enlargement from cardiac displacement due to a high diaphragm, for we have shown that in the right pectoral—left leg lead an inverted T wave is incompatible with considerable left ventricular enlargement, but is common in normal controls and in cases of cardiac displacement due to a high diaphragm. The right arm distal electrode is useless for this purpose. We have found no other major advantage in the left leg distal electrode, but there is one other minor advantage: if R is taller than S in the right pectoral—left leg lead, it may be concluded that there is dominance of the right ventricle. A similar finding in the right pectoral—right arm lead is suggestive but less certain.

The right arm distal electrode has been used extensively by Groedel (1934), was independently suggested by Roth (1935), advised by Larsen (1937), and favoured by Willcox and Lovibond (1937). Apart from its convenience it has two considerable advantages: first, normal standards are more uniform in that the T wave remains upright in all leads in adults, and is only rarely inverted in children and then only in the right pectoral lead; as a corollary, inversion of the T wave in the pectoral leads has much more significance with the right arm distal electrode than it has with the left leg; secondly, the P wave is upright and of adequate dimensions in leads paired with the right arm, whereas it is usually inverted and is very small in leads paired with the left leg. Although we have not drawn attention to the value of the right pectoral lead in studying disorders of rhythm, it may be remembered that Lewis (1909–10) found it expedient to use such a lead in his study of auricular fibrillation. Holzmänn (1937) found that abnormalities of the P wave could be well shown by placing the exploring electrode over the right auricle, and we have been using the right pectoral—right arm lead to demonstrate the tall sharp P wave associated with right auricular enlargement. There can be little doubt that the right arm is the better distal electrode for these purposes.

We conclude that the right arm is the distal electrode of choice for single or multiple chest leads for routine purposes, but for the special purpose of distinguishing left ventricular enlargement from cardiac displacement due to a high diaphragm we recommend the right pectoral—left leg lead.

MULTIPLE CHEST LEADS

The Cardiac Society of Great Britain and Ireland recommended a single chest lead, lead IV, for routine use, because it was considered that there was insufficient evidence upon which to recommend multiple chest leads.

Wilson and his associates, who have employed the multiple chest leads recommended by the American Heart Association, have concluded that anterior myocardial infarction will rarely escape detection if multiple chest leads are used in addition to the limb leads.

Holzmann (1937) used the chest leads in all types of heart disease, and found them useful in conditions other than myocardial infarction and angina pectoris. He advised the use of both the apical and the right pectoral lead, the latter being of aid in the diagnosis of right ventricular enlargement. Hecht (1936) came to a similar conclusion.

Groedel (1934) claims to have isolated the lævocardiogram and the dextro-cardiogram. The former is obtained with lead IV R, and the latter with a left sternal—right arm lead. Whether his theoretical considerations are right or wrong it is clear that considerable information may be gained by employing both these leads.

There can be no doubt that lead IV is an essential chest lead because it may be the only one to show evidence of myocardial infarction, especially by exhibiting a W complex or an inverted T wave. It is also certain that a monophasic downward initial ventricular complex indicating myocardial infarction may be restricted to the pectoral leads, and that, therefore, the left pectoral or a left pectoral lead is essential because this finding loses some of its significance in the right pectoral lead. In acute anterior myocardial infarction elevation of the RS-T segment is usually seen in both apical and left pectoral leads, but may be restricted to one or the other. If chest leads were only used in cases of possible ischæmic heart disease it is clear that both lead IV and a left pectoral lead should be employed.

But chest leads may be of value in other conditions such as rheumatic carditis, pericarditis, acute cor pulmonale from pulmonary embolism, left and right ventricular enlargement, bundle branch block, and for studying the form of the P wave and certain abnormalities of rhythm. For these purposes the right pectoral lead, or a combination of the right pectoral lead and one or both of the others, is required.

It is concluded that at least three chest leads may be used with advantage, not only because each has a function not shared by the others, but also because additional information may be gained by studying them in relation to one another.

The three chest leads which we have used were suggested by Roth (1935), and we have found them satisfactory. There are, however, two other favoured combinations of leads: the first is that used by Groedel (1934) and by Hecht (1936), and consists of two leads, one apical, the other basal, either just to the left of, or just to the right of the sternum, in the fourth intercostal space; the second is that recommended by the American Heart Association and consists

of a series of leads from the following points—the right border of the sternum in the fourth intercostal space, the left border of the sternum at the same level, midway between the latter and the point next to be described, the mid-clavicular line in the fifth intercostal space, the anterior axillary line at the same horizontal level, and the mid-axillary line, these leads being numbered from 1 to 6 with their appropriate prescript according to the distal electrode employed. The pre-scripts used to denote the distal electrode employed are : for the right arm—CR, for the left leg—CF, for the neutral electrode devised by Wilson and his associates—V. Thus the right pectoral lead which we have used would be called lead CR 1 when it is paired with the right arm, and CF 1 when it is paired with the left leg ; our left pectoral leads would be called leads CR or CF 3 approximately ; and our apical leads would be usually leads CR or CF 4 or 5. The letter C stands for “ chest.”

The choice between these three different combinations of multiple chest leads is no easy one. We have sufficient evidence to justify the use of three rather than two chest leads as a routine procedure when chest leads are requested. Because we have only used three chest leads we are unable to express an opinion as to the value of more. When the apex beat is within the anterior axillary line it is probable that three leads would be sufficient ; when it is further to the left there may be some advantage in four or even five leads. When only three leads are used it would seem more rational to employ the three suggested by Roth (1935), as described in this paper, rather than to lead from three fixed points on the chest wall.

SUMMARY AND CONCLUSIONS

1. The normal appearances of electrocardiograms obtained with lead IV R have been presented.
2. Five other chest leads were investigated : lead IV F ; the left pectoral—right arm lead ; the left pectoral—left leg lead ; the right pectoral—right arm lead ; and the right pectoral—left leg lead.
3. Limb lead and multiple chest lead electrocardiograms were obtained from 302 selected cases of heart disease, and from twelve cases of cardiac displacement due to a high diaphragm.
4. In addition to their value as an aid in the recognition of ischæmic heart disease, chest leads have been found of service in the diagnosis of rheumatic carditis, pericarditis, left ventricular enlargement, right ventricular enlargement, acute cor pulmonale resulting from pulmonary embolism, and of doubtful or bizarre forms of bundle branch block.
5. The right arm was both the most informative and the most convenient site for the distal electrode ; and we believe that the evidence is now sufficient to warrant its routine use in preference to the left leg. The latter was only advantageous when it was desired to distinguish left ventricular enlargement from cardiac displacement due to elevation of the diaphragm.
6. Multiple chest leads are of value not only because they may yield

diagnostic evidence of myocardial infarction when a single chest lead is barren, but also because they are a safeguard against faulty interpretation of lead IV, because each of the three leads (lead IV and the two pectoral leads) used in this investigation has some special value peculiar to itself, and because a study of these three leads in relation to one another may give information which is unobtainable by a study of individual leads.

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A NEW SIGN OF LEFT VENTRICULAR FAILURE

BY

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The prominent P wave associated with mitral stenosis is well recognized ; it is usually widened and is often notched, bifid, or flat-topped ; it is generally thought to be a result of left auricular hypertrophy. There is also some evidence that a tall spiked P wave may be produced by right auricular hypertrophy, for such a wave is rarely found except in cases of tricuspid stenosis, congenital pulmonary stenosis, and chronic cor pulmonale. It is the purpose of this communication to draw attention to a third type of P wave which we have found to be commonly associated with hypertensive heart disease, especially when there is left ventricular failure. This P wave is widened and of low voltage ; it is also usually bifid or flat-topped. Typical examples of these three types of P wave are shown in Figs. 1-3.

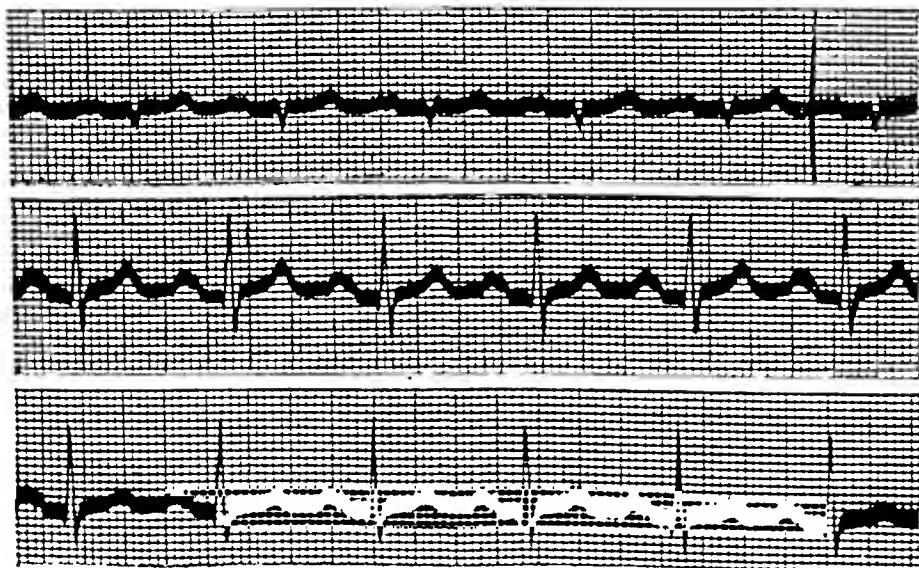


FIG. 1.—Prominent bifid and widened P wave in a case of mitral stenosis.

† Received July 28, 1938.

The normal P wave may be notched, but its duration does not exceed 0.1 sec. Its voltage in the favourable lead rarely exceeds 0.25 mv. and averages a

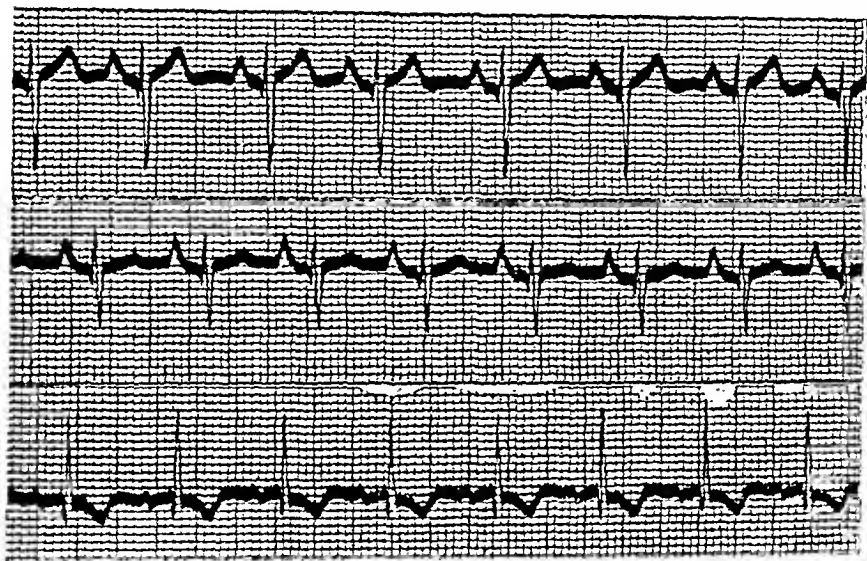


FIG. 2.—Tall spiked P wave in a case of chronic cor pulmonale (proved at autopsy).

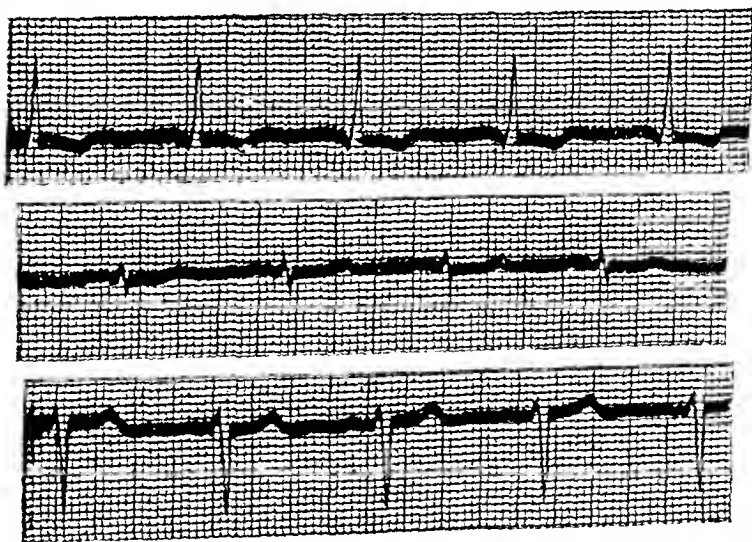


FIG. 3.—Wide bifid P wave of the low voltage in a case of hypertensive heart disease with left ventricular failure.

little under 0.15 mv. The P wave to which we are drawing attention commonly measures 0.12 sec. in duration and rarely more than 0.1 mv. in amplitude:

In a series of 1000 consecutive routine electrocardiograms this P wave was

found in 25 instances, or in 2.5 per cent. Four of these were cases of aortic valvular disease, and the remainder were cases of hypertensive heart disease. In the same series there were 25 instances of abnormal P waves associated with mitral stenosis, and five instances of tall spiked P waves with chronic cor pulmonale or with congenital pulmonary stenosis. It is therefore evident that this P wave is as common as the P wave of mitral stenosis, and about five times as common as the tall spiked P wave associated with chronic cor pulmonale or with congenital pulmonary stenosis.

To determine the significance of this P wave, we studied 70 patients with hypertensive heart disease and 25 with uncomplicated aortic valvular disease in various stages of development. As a control group we used 25 patients with ischæmic heart disease without cardiac enlargement. They were examined clinically, radiologically, and electrocardiographically, and no one was included where the diagnosis was in doubt. We divided the patients with hypertensive heart disease and those with aortic valvular disease into five groups which were determined as follows :

- Group A .. Those with no symptoms.
- Group B .. Those with slight effort dyspnœa.
- Group C .. Those with moderate or severe effort dyspnœa.
- Group D .. Those with left ventricular failure.
- Group E .. Those with right ventricular failure.

The diagnosis of left ventricular failure was made upon the presence of several of the following criteria : orthopnœa, paroxysmal cardiac dyspnœa, pulmonary œdema, persistent bilateral basal pulmonary rales, prolongation of the arm to tongue circulation time, radiological evidence of pulmonary congestion, pulsus alternans and gallop rhythm without bundle branch block. The diagnosis of right ventricular failure was made upon the finding of engorgement of the veins of the neck with enlargement and tenderness of the liver. The presence of dropsy was not considered essential for the diagnosis of right ventricular failure, nor was the latter diagnosis necessarily made because there was dropsy. Of course, all patients with failure of the right ventricle also had failure of the left ventricle.

The electrocardiograms were then analysed with regard to the P waves. These were classified as normal if they lasted for less than 0.1 sec., as doubtful if from 0.1 to 0.11 sec., and as widened if they exceeded 0.11 sec. We considered that the width of the P wave was the essential feature. Widened P waves occurred most frequently in lead II, but were often found in more than one lead. In some cases the bifid nature of P was so marked as to warrant the term "double P wave," for it consisted of two separate deflections, the one immediately following the other and each measuring 0.06 sec. in duration.

The results of this study are presented in Table I. In the hypertensive cases the incidence of a widened P wave increased from zero in the symptomless group to 61 per cent. in the group with left and right ventricular failure. It is important to note that there was no real difference in the incidence of a widened P wave in the group with left ventricular failure alone and the group with left and

right ventricular failure. Similar, but less convincing, results were obtained in the cases of aortic valvular disease. In the control group of 25 cases of ischaemic heart disease a widened P wave did not occur.

TABLE I.—RELATIONSHIP OF WIDTH OF P AND DEGREE OF CARDIAC FAILURE

	CLASS	P WAVE			NO. OF CASES
		>0.11"	0.1—0.11"	<0.1"	
Hypertensive heart disease ..	A	—	—	6 (100%)	6
	B	1 (4%)	—	23 (96%)	24
	C	2 (15%)	4 (30%)	7 (55%)	13
	D	7 (50%)	2 (14%)	5 (36%)	14
	E	8 (61%)	1 (8%)	4 (31%)	13
Aortic valvular disease ..	A	—	—	—	0
	B	—	2	1	3
	C	—	2	5	7
	D	3	2	3	8
	E	1	—	4	5
Ischaemic heart disease		—	2	23	25

It is evident that the type of P wave which we have described is commonly associated with left ventricular failure.

DISCUSSION

The cause of the abnormal P waves in mitral stenosis has been discussed by several authors. Although von Boros and Trendelenburg believe that an intra-auricular conduction defect is responsible, the majority think that the explanation lies in hypertrophy of the left auricle. Some attempts have been made to diagnose from the lead in which the notched P wave occurs (Winternitz) or from the shape of the notching (Holzmann) which auricle is affected, but there is insufficient evidence for these views. In a recent study, Berliner and Master tried to correlate electrocardiographic and post-mortem findings in cases of mitral stenosis. They found hypertrophy of the left auricle in cases with bifid and widened P waves, and hypertrophy of the right auricle in addition in cases in which the P wave was increased in height. Their tallest P waves occurred in cases of combined mitral and tricuspid stenosis. They suggested that a tall P wave might result from a summation effect from hypertrophy of both auricles. Because we are familiar with the tall spiked P wave associated with pulmonary stenosis and chronic cor pulmonale, and because we have noticed that, though tall, the P wave is not widened in these conditions, we suggest that an increase in voltage of the P wave may indicate hypertrophy of the right auricle, whereas widening and notching of the P wave may indicate hypertrophy of the left auricle.

If this view should prove correct, then there is a ready explanation for the wide bifid P wave associated with left ventricular failure, for in this condition an

increased stress falls upon the left auricle. It is tempting to suggest that this type of P wave is yet another sign, and an early one, of left ventricular failure, to be ranked with gallop rhythm.

This is but a preliminary report and is published in the hope that it may stimulate investigation in this field. With the aid of an œsophageal lead, a semi-direct right auricular lead, and careful clinical and post-mortem investigation it should not be difficult to solve the problem. We already have evidence that chest leads taken from the right border of the sternum and paired with the right arm electrode may yield a tall spiked narrow P wave in cases with hypertrophy of the right auricle.

SUMMARY

1. A widened P wave of low voltage, usually bifid or flat-topped, has been found in association with left ventricular failure in cases of hypertensive heart disease and of aortic incompetence.

2. It is suggested that this P wave results from left auricular stress.

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THE SIGNIFICANCE OF ELECTROCARDIOGRAMS SHOWING A "SECOND POSITIVE WAVE OF QRS" IN LEAD III

BY

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During the past two years an investigation has been made to determine whether electrocardiograms showing anomalous forms of QRS in lead III have any diagnostic or prognostic importance. Several distinct types of anomalous QRS3 have been encountered, and the findings in one of these types have already been published ("Large Q3," Peel, 1938). It is now proposed to consider a second variety in which the R and S deflections are followed by a third wave directed upwards and pointed. Katz and Slater (1935) have named this "the second positive wave of QRS3" and specify the following criteria for its recognition :

1. The standardization must show no "overshoot."
2. R3 must be a positive wave above the iso-electric line.
3. R3 must be followed by a definite S3, the amplitude of which may vary.
4. The upstroke of S3 must rise above the iso-electric level to a positive peak, and then descend either suddenly or gradually to the iso-electric level ; this peak may or may not be notched.

Katz and Slater collected 320 examples from a series of 8000 electrocardiograms and published a preliminary report on 50 of them, including post-mortem records in three cases. Clinical evidence of organic disease was present in 86 per cent., and they concluded that the abnormality should be regarded as indicative of organic myocardial disease.

Hope Gosse and Lowe (1937) found complexes of this type in 2.2 per cent. of all their cases, and published an analysis of 44 ; they arrived at a conclusion diametrically opposed to that of Katz and Slater : "Of this 2.2 per cent. the cases were almost equally divided between hearts diagnosed as clinically normal and those in which myocardial damage was considered to be present. . . . As a result of this investigation we do not find that any diagnostic importance can as yet be placed upon this variation from the average normal ventricular complex."

Although these are the only publications which deal directly with the type

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of complex in question, certain others have an indirect bearing on the subject. Katz and Slater admit any electrocardiogram in which lead III fulfils their requirements, irrespective of the presence or absence of abnormality in the remaining leads and irrespective of the breadth of the QRS complex. Some electrocardiograms which have been described as examples of right branch bundle block conform to their definition in so far as QRS3 is concerned, though it is true that Wilson's (1934) original description of what has since been termed "the common variety of right branch bundle block" fails to fulfil their second condition, as there is no initial R3. V. Deesten and Dolganos (1934), however, include some records with and some without an initial R in their description of "atypical branch bundle block with a favourable prognosis"; those with an initial R satisfy all of Katz and Slater's criteria. It is of interest to note that the single illustration published by Hope Gosse and Lowe has a broad QRS measuring 0.12 sec., with a broad S in leads I and II corresponding in time to the "second positive wave" of lead III; it differs from Wilson's description of branch bundle block only in the presence of the initial R3.

Another article germane to the subject is by Bland and White (1931), entitled "The clinical significance of complete inversion of lead III." Admittedly the electrocardiogram illustrated shows no "second positive wave"; it has inverted P and T waves, small R and large S. It is clear, however, that the appearance of the QRS complex resulting from inversion will vary from case to case according to the deflections originally present. A complex consisting of Q and R will become R and S after inversion; one in which the original deflections are R and S will show Q and R; while inversion of an electrocardiogram with Q, R, and S will produce a complex consisting of R, S, and a "second positive wave."

Bland and White had 115 cases which they considered to show complete inversion of lead III. Organic disease was only present in 55 per cent. as compared with 82 per cent. of their total patients. On the other hand, 72 per cent. of those with inversion of lead III had some condition liable to produce a transverse lie of the heart, and the abnormality was often abolished by deep inspiration. They conclude that an electrocardiogram showing complete inversion of lead III is usually associated with a transverse lie of the heart and has little clinical significance. Proger (1931) described electrocardiograms similar to those discussed by Bland and White as occurring frequently in obesity. It may be recalled that Hurxthal (1933) suggested that a "large Q3" in many instances represented an "inverted R." We have previously shown (Peel, 1938) that electrocardiograms with a large Q3 can be subdivided into two groups, one of which is closely associated with coronary disease (Q2 present), while the other is frequently found in obese patients and is in many cases related to a transverse lie of the heart (Q2 absent). If Hurxthal's suggestion is accepted, the findings relative to this second group are brought into line with those of Bland and White.

It seems reasonable to suggest that the discrepancy between the conclusions of Katz and Slater and those of Hope Gosse and Lowe may to some extent be explained on the assumption that electrocardiograms showing a "second positive wave" in lead III are not all identical. Some may represent branch

bundle block, implying organic myocardial disease ; others may correspond to Bland and White's "inversion of lead III," and be associated with a transverse lie of the heart ; and there may well exist yet other types. Another possible explanation of the difference found in the two series may lie in the nature of the material from which the cases were drawn.

In dealing with the present series, we propose to use the symbol "R'" for the "second positive wave of QRS", examples of which are shown in Figs. 1 and 2. We have analysed 1200 consecutive cases from our original material

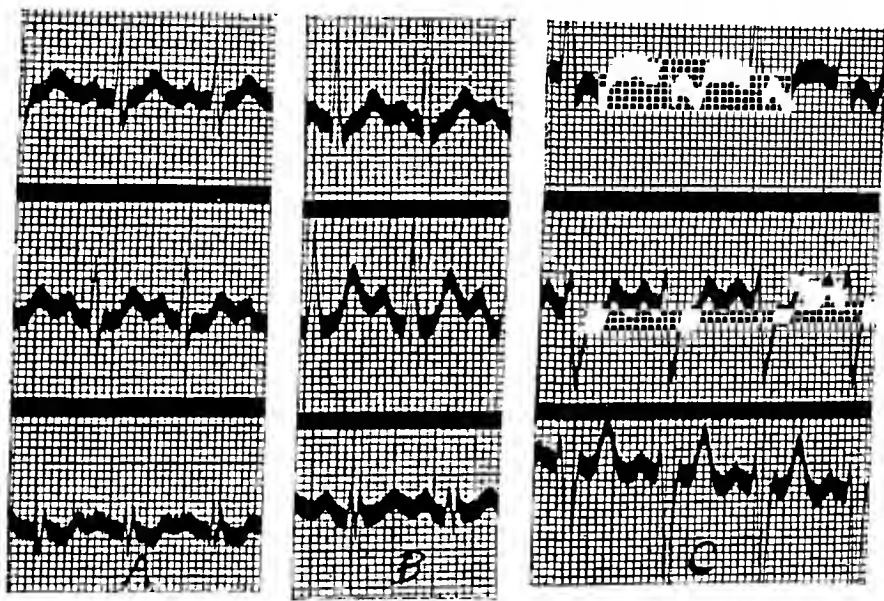


FIG. 1.—Examples of QRS3 showing a "second positive wave" and R3 exceeding 2 mm. in height. Type associated with a high incidence of organic disease and high mortality, irrespective of the presence of other electrocardiographic abnormality.

- A. Electrocardiogram otherwise normal. Male, 41, hypertensive heart disease.
- B. Electrocardiogram otherwise normal. Female, 21, mitral endocarditis.
- C. Electrocardiogram otherwise abnormal. Male, 59, cardio-aortic syphilis and effort angina.

so as to compare the incidence of organic disease in patients with an "R'" in lead III, with that in the total series. Next we have extracted those patients whose electrocardiograms were completely normal and compared them with those whose only electrocardiographic abnormality consisted of an "R'" in lead III. We have investigated the influence of other features in the electrocardiogram in determining the diagnostic and prognostic significance of the abnormality. We have looked into the possibility of differentiating complexes with an "R'" into two or more groups which might differ in their import. Finally in those of our cases in whom serial electrocardiograms are available, we have studied the conditions under which "R'" has appeared or disappeared.

ANALYSIS OF RESULTS

The material from which our examples were obtained consists of 1307 patients examined during the years 1928-1933. An analysis of 1200 consecu-

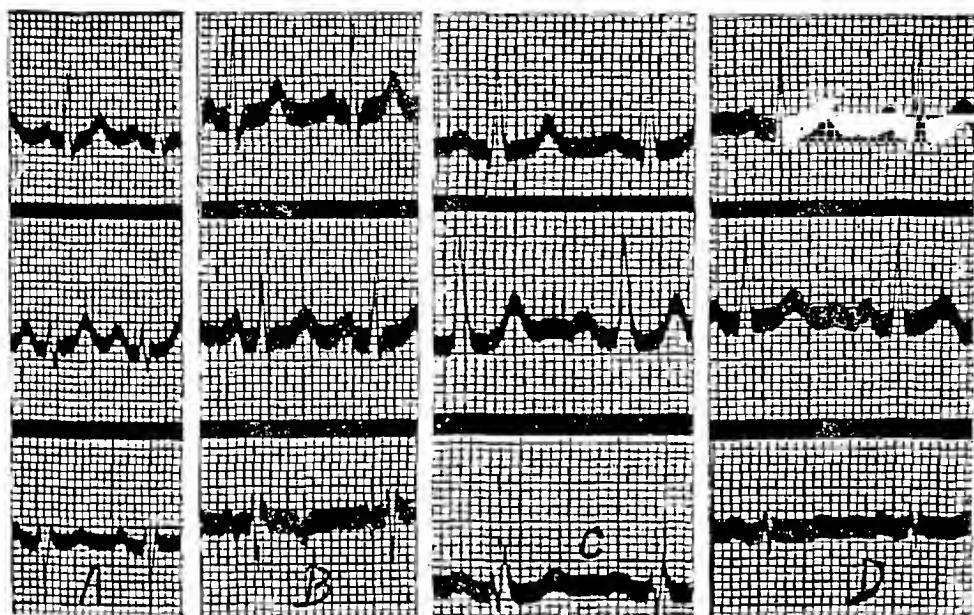


FIG. 2.—Examples of QRS3 showing a “second positive wave” and R3 small (less than 2 mm.) Type associated with a lower incidence of organic disease and low mortality provided the electrocardiogram is otherwise normal.

- A. QRS3 resembling a normal complex which has been inverted, but P3 and T3 are upright. Male, 64, no organic heart disease.
- B. QRS3 resembling an inverted normal complex; P3 and T3 also inverted—“Complete inversion of lead III” (Bland and White, 1931). Female, 25, obese and neurotic.
- C. QRS3 showing small R and S with large “second positive wave.” A sparsely built man of 61 with a prominent abdomen.
- D. QRS3 showing all three deflections small. Male, 61, effort syndrome, no organic heart disease.

tive cases showed 28 per cent. in whom no certain evidence of organic cardiovascular disease was detected clinically and 72 per cent. with such evidence. Of these, 33 per cent. had infective lesions; 26 per cent. suffered from coronary disease, arteriosclerosis, or hypertension; 4 per cent. had primary pulmonary disease, and 4 per cent. thyrotoxicosis; the remaining 5 per cent. had miscellaneous conditions including myxædema, obesity, anæmia with cardiac complications, congenital lesions, etc.

We have 62 patients in whom the electrocardiogram has at some time shown an “R” in lead III, excluding one in whom it was only noted during paroxysms of ventricular tachycardia. Organic heart disease was recognized clinically in 51 cases (82 per cent.), a figure which agrees closely with that given by Katz and Slater. The incidence of organic disease is somewhat higher than in the total series, and the increase is confined to cases of coronary disease, arteriosclerosis, and hypertension; these account for 57 per cent., or more than double their

incidence in the total material. Rheumatic lesions were less frequent (14.5 per cent. as compared with 28 per cent.), while pulmonary disease and thyrotoxicosis showed no difference.

Two patients were labelled "doubtful" and nine (14.5 per cent.) were thought to be free from organic cardiac disease at the time of examination. It is difficult to exclude heart disease with certainty in these cases. Five were below the age of 45; two of them had mild hyperthyroidism, one had extrasystoles, one had fainting attacks which were regarded as *petit mal*, and one was an obese woman with acute cholecystitis and a rapid pulse. The remaining six were over 45; two had extrasystoles, in one case following an acute infection and accompanied by tachycardia and impaired exercise tolerance; on the other hand, two had a condition liable to produce a transverse lie of the heart (splenomegaly in one, diverticulosis in the other); and two suffered from a neurosis. It is significant that of the seven patients traced, three are working, a fourth is much improved, and the incapacity in one case is of nervous origin; one died six years after examination from a cause unknown; and the last died from acute circulatory failure following cholecystectomy. These cases may be summarized by stating that organic myocardial disease was probably present but unrecognized in one, that it may have been present in another who died, and that in three with extrasystoles there was a septic focus or recent infection which may have caused temporary myocardial damage. In the remaining six myocardial disease was probably absent; two of them had a condition liable to produce a transverse lie of the heart.

Of the 62 patients with an "R" in lead III, 45 have been traced (March 1938). Twenty-five patients have died and three are incapacitated, but in one of them the incapacity is nervous in origin. Nine have improved and eight are working.

The Influence of other Electrocardiographic Features

Many electrocardiograms with an "R" in lead III show some other abnormality in addition (see Fig. 3), and these fall into two groups. The first includes findings which would be regarded as significant irrespective of the presence of "R" (e.g. RT displacement, coronary T wave, branch bundle block or intraventricular block, auricular flutter, and auricular fibrillation); the second includes those which would be considered of little or no importance in the absence of "R" (e.g. abnormalities of the electric axis, slight notching of auricular or ventricular complexes, digitalis effects, inversion of P3 or T3, extrasystoles, and nodal escape).

There are 26 cases in which the electrocardiogram showed some "significant" abnormality as defined above in addition to an "R" in lead III. Organic disease was present in all, and the prognosis was extremely bad. Out of 22 patients traced, 20 are dead, one is incapacitated, and only one has improved. In the two living patients, the "R" and the other abnormality were not present simultaneously, but succeeded one another. When an "R" and another significant abnormality were present simultaneously, all the cases traced have died (19 out of 23).

In 36 of our patients the electrocardiogram was normal except for the presence of an "R'" in lead III. For comparison with these we have collected 352 cases from the same original material in whom the electrocardiogram was

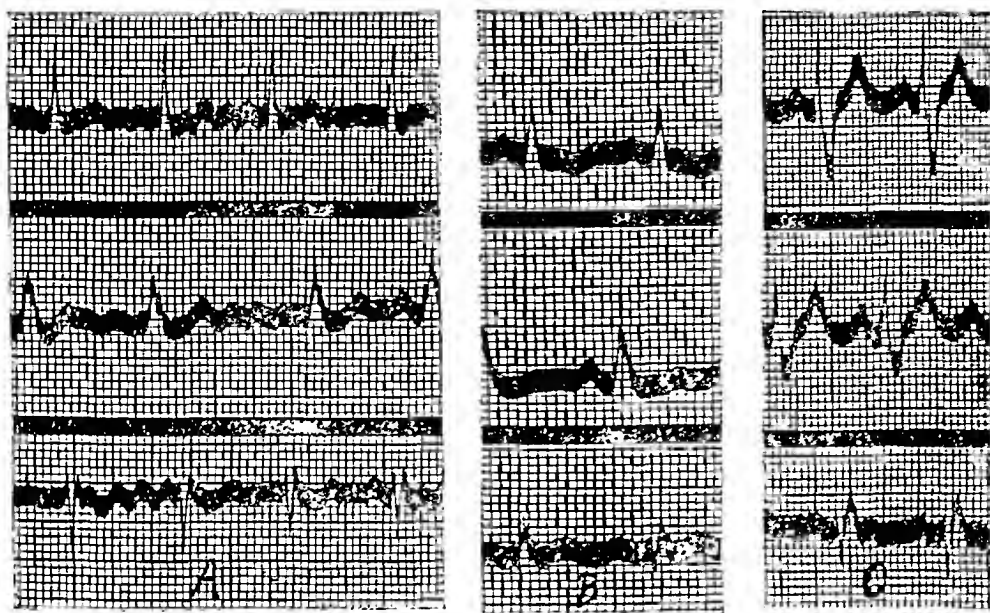


FIG. 3.—Examples of QRS3 showing a "second positive wave" and R3 small, but electrocardiogram otherwise abnormal. Type associated with high incidence of organic disease and high mortality.

- A. QRS3 resembling an inverted normal complex. A sparsely built man of 59 with auricular fibrillation.
- B. QRS3 with minute R and S and prominent "R'" T1 inversion. Male, 62, hypertension.
- C. Wilson's type of right bundle branch block, showing in lead III a small initial R, S, and broad "R'." The electrocardiogram fulfils Katz and Slater's criteria. Male, 57, with chronic coronary disease and congestive failure.

normal and showed no "R'" in lead III. Organic heart disease is very much more frequent in those with an "R'3" than in those without (70 per cent. as compared with 43 per cent.), and the increase is accounted for entirely by cases of coronary disease, of arteriosclerosis, or of hypertension; these comprised 42 per cent. as compared with 8 per cent. in patients with normal electrocardiograms. Rheumatic lesions were slightly less frequent, while the incidence of other forms of heart disease was approximately the same.

We have no follow-up figures available for the patients whose electrocardiograms were completely normal. Of the 36 whose only abnormality was an "R'" in lead III, 23 have been traced. Five are dead and two are incapacitated; eight have improved and eight are able for work. The prognosis is very much better than when the electrocardiogram shows some "significant" abnormality in addition to an "R'" in lead III.

We have attempted to determine whether there are any electrocardiographic features which will enable the diagnostic or prognostic value of an "R'" to be

gauged when no other "significant" abnormality is present. If a relationship exists between some of these cases and Wilson's type of bundle branch block, it might be thought that the presence or absence of an S in lead I would help in their differentiation. This is not the case, there being no appreciable difference between the cases with and those without an S1. Having previously shown the importance of Q2 in assessing the diagnostic value of electrocardiograms with a "large Q3," it was thought that Q2 might also help in evaluating those with an "R'" in lead III. There is, however, no significant difference in the incidence of organic lesions, the incidence of coronary disease, the mortality rate, or the recovery rate, when groups with and without a Q2 are compared.

There is evidence that the character of QRS3 itself may be of diagnostic and prognostic importance. Katz and Slater's definition is compatible with wide variations in the actual form of the complex; any one deflection (R, S, or "R'") may be prominent with the other two small; any two may be prominent with the third small; all three may be large, or all three may be small. Thus there are eight possible subgroups, each of which we have investigated individually. It was found that in every group with a prominent initial R (exceeding 2 mm. in height) organic disease was always present and the mortality was high—75 per cent. for the whole group and 50 per cent. even when "R'" was the only significant abnormality in the electrocardiogram (see Fig. 1). On the other hand in every group with a small initial R (less than 2 mm. in height) (see Fig. 2) there were a number of patients who were thought to be free from organic disease, and the mortality rate was much lower—45 per cent. for the whole group and only 12 per cent. when the electrocardiogram was otherwise normal. All eight patients who recovered working capacity and seven of the remaining nine who improved belong to the group with a small initial R and no other abnormality in the electrocardiogram.

This finding is of considerable importance in view of Bland and White's conclusions regarding "total inversion of lead III"; for in one of the groups defined above, namely, that with a small R, large S, and small "R'," the complex exactly resembles a normal QRS which has been inverted; P3 and T3 were only inverted in about half the cases. If it is justifiable to regard these as "inverted QRS complexes," the significance of the large initial R in the other group can be explained on the assumption that it represents inversion of a complex which originally showed a large Q3, a suggestion made by Hurxthal in 1933.

The electric axis is not strictly comparable with the height of R in lead III for some cases with a "prominent" initial R3 show left axial deviation, while some with a small R3 have a normal axis. When an "R'" in lead III is the only abnormality in the electrocardiogram, there is little difference between those with a normal axis and those with left axial deviation, either in the incidence of organic disease, the mortality rate, or the recovery rate. On the other hand, left axial deviation is more common than a normal axis when other significant abnormalities are present in the electrocardiogram; since the mortality rate is very much higher in the latter circumstances, it follows that

the prognosis is worse with left axial deviation than with a normal axis, when the remaining features of the electrocardiogram are not taken into account.

As was found to be the case with electrocardiograms showing a large Q3, the breadth of QRS is an extremely important prognostic feature in those with an "R'" in lead III. The ultimate fate of 45 patients traced is compared in the table with the breadth of their QRS complexes. The mortality rate rises steadily and the recovery rate falls steadily as the breadth of QRS increases ; and there is such a close parallel between this series and the "large Q3" series previously published that repetition of the latter figures seems justifiable for comparison.

Even when electrocardiograms which show other abnormalities are excluded, the breadth of QRS is still important for prognosis. This procedure considerably reduces the number with a broad QRS, as it cuts out all cases with bundle branch block or intraventricular block. We have traced 23 patients who had an "R'" in lead III but no other significant abnormality. In seven, QRS was less than 0.08 sec. ; six are either improved or working and one is dead. In 16, QRS measured 0.08 or more ; four are dead and two are incapacitated, six have improved and four are working.

TABLE I
THE INFLUENCE OF THE BREADTH OF QRS

	CASES TRACED	DEAD, PER CENT.	INCAPACITATED, PER CENT.	IMPROVED OR WELL, PER CENT.
QRS below 0.08				
Large Q3	13	23	15	62
Present series	9	22	0	78 (44 working)
Total	22	22	9	68
QRS=0.08 sec.				
Large Q3	14	43	28	28
Present series	18	55	11	33 (11 working)
Total	32	50	18	31
QRS above 0.08				
Large Q3	15	73	13	13
Present series	18	72	6	22 (11 working)
Total	33	72	9	18

The Appearance or Disappearance of an "R'" in Lead III

In four of our cases an "R'" has appeared in lead III while the patient was under observation. They are as follows :

1. An obese woman of 36 with acute cholecystitis ; the development of "R'" coincided with the onset of fatal circulatory failure immediately after operation.

2. A man of 30 with syphilitic aortitis, angina of effort, and gross RT depression in all leads of the electrocardiogram. "R'" appeared three weeks later, when RT had returned to the iso-electric level. A few hours after this record was obtained, he died suddenly. Post-mortem examination showed oedematous swelling of syphilitic plaques, producing almost complete occlusion of both coronary orifices, and the right circumflex branch contained a fresh thrombus; microscopic examination showed an interstitial myocarditis of older date.
3. A stout woman of 54 with hypertension and congestive failure had a falling blood pressure along with the electrocardiographic changes of coronary disease. At one stage there was an "R'" in lead III. Later the initial R disappeared, leaving S and "R'" only, accompanied by inversion of T1. She improved temporarily, but died from congestive failure three years later.
4. A man of 54 with hypertension developed auricular flutter during an attack of lobar pneumonia. "R'" appeared when the normal rhythm recurred spontaneously a few days after the crisis. Seven years later auricular fibrillation was present and "R'3" had disappeared; despite the fibrillation his capacity for effort was better than when he was convalescent from the pneumonia.

TABLE II
INCIDENCE OF HEART DISEASE EXPRESSED AS PERCENTAGES, AND
FOLLOW-UP RESULTS

CLINICAL FINDINGS AND FOLLOW-UP RESULTS	1,200 CONSECUTIVE CASES FROM ORIGINAL MATERIAL	352 CASES WITH NORMAL ELECTROCARDIOGRAM FROM SAME ORIGINAL MATERIAL	62 CASES WITH "SECOND POSITIVE WAVE OF QRS" ("R'3")	36 CASES WITH "R'3" AS THE ONLY ABNORMALITY	26 CASES WITH SOME OTHER SIGNIFICANT ABNORMALITY IN ADDITION TO "R'3"	18 CASES WITH "R'3" AND PROMINENT INITIAL R (EXCEEDING 2 mm.)	7 CASES WITH "R'3," LARGE INITIAL R, AND NO OTHER ABNORMALITY	44 CASES WITH "R'3" AND SMALL INITIAL R (UNDER 2 mm.)	29 CASES WITH "R'3," SMALL INITIAL R, AND NO OTHER ABNORMALITY	14 CASES WITH QRS OF LESS THAN 0.08 SEC.	28 CASES WITH QRS OF 0.08 SEC.	20 CASES WITH QRS OF MORE THAN 0.08 SEC.
Organic disease :												
Rheumatic, per cent. . .	28	22	14	17	13	16	14	14	14	29	11	10
Syphilis and other infections, per cent. . .	5	1	3	0	8	0	0	4	0	0	7	0
Coronary disease Arteriosclerosis, Hypertension, per cent. . .	26	8	57	42	75	78	72	48	38	29	54	80
Pulmonary, Thyrotoxic, Others, per cent. . .	13	12	8	11	4	6	14	9	10	21	7	0
Total organic, per cent. . .	72	43	82	70	100	100	100	75	62	79	79	90
No organic lesion, per cent.	28	57	18	30	0	0	0	25	38	21	21	10
Cases traced.	—	—	45	23	22	16	6	29	17	9	18	18
Dead, per cent. . .	—	—	55	22	90	75	50	45	12	22	55	72
Incapacitated, per cent. . .	—	—	7	6	5	12½	17	3	0	0	11	5
Improved, per cent. . .	—	—	20	36	5	12½	33	24	41	33	23	11
Able for work, per cent.	—	—	18	36	0	0	0	28	47	44	11	11

In each of these four cases there are good grounds for associating the appearance of an "R'" in lead III with the existence of an active pathological process affecting the myocardium.

In eight of our cases an "R'" has disappeared at a later date. Its disappearance has only occurred while under observation in three cases. Two were cases of severe rheumatic carditis in which "R'" was present during the acute stage and vanished as convalescence became established; one of the patients made a good recovery, but the other was left with an adherent pericardium and died three years later. The third case was one of coronary disease with congestive failure, who became slowly worse and died two weeks after "R'" had gone; this is the only case in which its disappearance was not associated with at least temporary improvement. In the remaining five cases, the patient's capacity for effort was improved when on re-examination some years later "R'" was no longer present.

SUMMARY AND CONCLUSIONS

1. Organic heart disease is more common in patients whose electrocardiograms show a "second positive wave of QRS3" than in the material from which these cases were collected (82 against 72 per cent.). Many of these electrocardiograms show some other significant abnormality, in which case organic disease is always present, and the mortality since 1928-1933 has been 90 per cent.

2. Organic lesions are much more frequent in patients whose sole electrocardiographic abnormality consists of a "second positive wave of QRS3" than in patients whose electrocardiograms are completely normal (70 per cent. against 43 per cent.). The increase is due to a greater number with coronary disease, hypertension, or arteriosclerosis (42 per cent. against 8 per cent.).

3. Where it has been possible to fix the time of appearance of the "second positive wave of QRS3," this has occurred when an active pathological process was affecting the myocardium. In seven out of eight cases in which it ultimately disappeared, the patient's capacity for effort improved, at least temporarily.

4. When a "second positive wave of QRS3" is the only electrocardiographic abnormality, the shape of the complex is important for diagnosis and prognosis, and its breadth gives further assistance in prognosis.

5. As regards the shape of the complex, the height of the initial R is the determining factor. When this was a prominent deflection exceeding 2 mm. in height, organic disease was always present; and the mortality in cases with an otherwise normal electrocardiogram was 50 per cent. When the initial R was a small deflection of less than 2 mm. in height the incidence of recognizable organic disease was only 62 per cent. and the mortality in cases with an otherwise normal electrocardiogram was only 12 per cent.

6. The breadth of QRS gives little help in diagnosis, but is of great importance in prognosis. The mortality rises steadily from 22 per cent. with a QRS below 0.08 sec., to 55 per cent. at 0.08 sec., and to 72 per cent. above 0.08 sec.

These mortality figures are almost identical with those found in dealing with another series of electrocardiograms where the abnormality was a "large Q3." The significance of the breadth of QRS therefore appears to be independent of the nature of any abnormality which may be present.

I am greatly indebted to Miss A. Miller, almoner at the Victoria Infirmary, for her valuable help in tracing patients ; to Drs. G. J. Wilson and A. E. S. Melville with the staff of the X-ray department ; to Dr. John Anderson, pathologist ; to the members of the medical and surgical staff ; and to the numerous practitioners who have kindly furnished information regarding their patients.

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SOME NOTES ON THE CARDIAC CLUB

BY

JOHN COWAN AND OTHERS

"The Sun of our body, the King and sole Commander of it." —
"Anatomy of Melancholy."

It is difficult to convey to the Georgian a proper impression of the attitude of the late Victorians to heart disease. Laennec's discovery of auscultation dominated the succeeding fifty years, and towards the end of the century the characteristic sounds of the various valvular lesions had been fully elucidated. For a time medicine stagnated. Those of us who were Residents in medical wards viewed the outlook with dismay, for the progress of surgery at that time, under the influence of Lister's work, was phenomenal. But better times were at hand.

The physiological laboratories were at work under Gaskell and others. The bacteriologists were turning their attention to medical subjects; the tubercle bacillus was discovered by Koch. X-rays showed the contents of the thorax. The sphygmomanometer was adapted for clinical use, and the polygraph and later the electrocardiograph added their quota to the general store.

But, although new methods of investigation became available, a personal influence was needed to speed up the work, and James Mackenzie became the centre of the picture. He had many facets. A tall, burly man, with all the directness of the North, he seemed at first sight rather dictatorial and overbearing; but his transparent goodwill, his unselfishness, and his humility soon made manifest that it was merely his intolerance of sham, and his search for truth. His intensive study of the Shorter Catechism had inculcated a downright mode of expression! He took a kindly interest in all his neighbours, especially the younger members of his profession; and he was always receptive of opinions based upon material which was outwith his own opportunities. Before long he had attracted to himself many men who were interested in the problems of heart disease; and had himself suggested to some of our members that a small club should be formed for meetings and discussions. The Cardiac Club was conceived in Burnley.

Another European war came, and our profession was scattered over the world. It was not a great war, for it altered little save garden fences, but it left a terrible swathe behind it. Many men had died, and many more were suffering in health, from wounds or sickness, for whom provision was required. During the war the Pension Service was necessarily a makeshift; the staff was insufficient and inexperienced, and their decisions needed revision and co-ordination. Many of the cases were cardiac, at least in name, so, in April 1920, the Ministry appointed Consultants to aid the Regional Directors in the assess-

ment and treatment of the cardiac patients. The majority of those appointed had been associated with James Mackenzie before the war.

In 1921 a conference of the Consultants was held in London, and others subsequently. They were mainly concerned with the technical and administrative difficulties of the Ministry, but several interesting discussions upon purely medical subjects took place, and some valuable statistical data were collected. The influence of war service as a cause of subacute bacterial endocarditis ; the effects of malaria upon the myocardium ; the incidence of syphilitic disease of the heart ; the causes of death in chronic valvular disease ; the value of quinidine in auricular fibrillation, etc., were considered.

The conferences were appreciated by those concerned (Carey Coombs, T. F. Cotton, John Cowan, Ivor Davies, Wardrop Griffith, John Hay, W. E. Hume, Thomas Lewis, J. E. MacIlwaine, W. T. Ritchie, Robert Sevestre, H. J. Starling), who felt that they had been of service to themselves and perhaps to cardiac science, and that it was desirable that they should be continued under different auspices. On February 21, 1922, Hume wrote to Cowan (apparently considering him to be the most senior of the group, though Wardrop Griffith was in reality the doyen) suggesting that the men interested in heart disease should be called together at the next meeting of the Association of Physicians. Accordingly a meeting took place at Oxford, with A. G. Gibson in the chair, and on April 22, 1922, the Cardiac Club was born. The official accoucheurs were Carey Coombs, T. F. Cotton, John Cowan and W. E. Hume. The first active meeting of the Club took place in London later that year. A list of the original members and of those elected subsequently follows, with the dates of election of the extra-ordinary members.

THE CARDIAC CLUB

HONORARY MEMBER

James Mackenzie, F.R.S., Kt., 1915

Extra-Ordinary
Member

ORIGINAL MEMBERS

1922	Carey F. Coombs	-1932	
	T. F. Cotton		
	John Cowan (<i>Secretary</i> , 1922-25)		1930
	J. G. Emanuel		1933
	A. G. Gibson (<i>Secretary</i> , 1925-28)		
	T. Wardrop Griffith, C.M.G.		1928
	John Hay		1935
	Thomas J. Horder, K.C.V.O., Kt. 1918, Bt. 1923, Baron 1933		1933
	W. E. Hume, C.M.G.		
	Thomas Lewis, C.B.E., F.R.S., Kt. 1921.		1927
	J. E. MacIlwaine,	-1930	
	John Parkinson		
	W. T. Ritchie, O.B.E. (<i>Treasurer</i> , 1922-31)		1932
	H. J. Starling		
	K. D. Wilkinson, O.B.E.		

THE CARDIAC CLUB—*continued*

MEMBERS ELECTED SUBSEQUENTLY

- 1923 J. Crighton Bramwell (*Secretary*, 1928–32)
Francis R. Fraser
- 1924 A. N. Drury, F.R.S.
C. E. K. Herapath, M.C.
- 1925 A. M. Kennedy
S. Wentworth Patterson
- 1926 George A. Allan
Maurice A. Cassidy, C.B., K.C.V.O., Kt. 1934
- 1927 S. B. Boyd Campbell, M.C.
Arnold W. Stott
- 1928 H. Wallace Jones
D. Evan Bedford (*Secretary*, 1932–36)
- 1930 E. P. Poulton
- 1931 J. Maurice Campbell, O.B.E. (*Secretary*, 1936–37)
- 1933 R. T. Grant, F.R.S.
A. R. Gilchrist
- 1934 Leonard Abrahamson
C. W. Curtis Bain, M.C.
- 1936 C. Bruce Perry

Of these original members, three have died : Carey Coombs in his full vigour in 1932, MacIlwaine of Belfast in 1930, and James Mackenzie in 1925. At their next meeting the Club put on record this expression of appreciation of their only Honorary Member ; and short notes of the dates and appointments of these three members follow.

Minute of the Cardiac Club, May 28, 1925

“ The Cardiac Club laments the death, on January 26, 1925, of its Honorary Member, Sir James Mackenzie. By the power of his genius and the wealth of his achievements he exercised a vast influence upon the branch of Medicine with which his name is indissolubly associated ; and his pre-eminence, transcending the limitations of race and clime, was universally acknowledged. So long as the Science of Medicine endures so long will the name of Sir James Mackenzie be honoured.

“ This tribute is rendered to the memory of him whom all Members of the Cardiac Club revered as their Master ; and the Club respectfully offers its sincere sympathy to Lady Mackenzie and Miss Mackenzie in the great loss which they have sustained.”

JAMES MACKENZIE, 1853-1925

M.B., 1878 ; M.D., 1882 ; F.R.C.P., London, 1913. F.R.S., 1915. LL.D., Aberdeen, 1910 ; Edinburgh, 1911. Knight, 1915. Hon. Physician to H.M. the King in Scotland, 1920.

Physician, Victoria Hospital, Burnley ; 1880-1907. Physician, Mount Vernon Hospital for Diseases of the Chest ; 1910-18. Physician to the Cardiac Department, London Hospital, 1911-18. Director of the St. Andrew's Institute of Clinical Research, 1918-25. Schorstein Lecturer, 1911. Oliver Sharpey Lecturer, 1911. George A. Gibson Lecturer, 1914.

CAREY FRANKLIN COOMBS, 1879-1932

M.B., 1901. M.D., 1903. F.R.C.P., 1917.

Physician, Bristol General Hospital, 1920. Director, Bristol University Centre of Cardiac Research, 1927.

Major, R.A.M.C., T.F. Served in England, Egypt, Mesopotamia and France, 1914-19. Long Fox Memorial Lecturer, 1925. Chadwick Lecturer, 1927. Lumleian Lecturer, 1930.

JOHN ELDER MACILWAINE, 1874-1930

B.Sc. (Engineering) 1894. M.B., 1901 ; M.D., 1904 ; D.P.H., 1907.

Physician, Royal Victoria Hospital, Belfast, 1910-29. Professor of Materia Medica and Therapeutics, Queen's University, Belfast, 1921-28.

Irish Rugby International, 1897-99.

Dresser, Irish Hospital, South Africa, 1899-1900. Physician, St. John's Ambulance Brigade Hospital, France, 1915-17.

The First Annual Meeting of the Cardiac Club was held at University College Hospital, London, under the chairmanship of Sir Thomas Lewis on November 22, 1922 and, subsequent meetings have been held on the day previous to the annual meetings of the Association of Physicians, wherever the Association happened to meet.

Many subjects have been discussed by the Club: the heart in the acute infections ; hyperpirosis ; angina pectoris ; infarct of the heart ; heart block ; the heart in pregnancy ; cardiac asthma ; vaso-vagal attacks ; the treatment of œdema ; etc. In addition to the set subjects many short discussions upon case records, electrocardiograms, pathological specimens, etc., have also taken place, to the obvious pleasure of the members. On several occasions demonstrations have been given to the Club by those working in the laboratories. A list of the main subjects discussed at each meeting follows with the names of those who introduced the discussion.

In addition to the value the members have received from the meetings, the most important function of the Club has been the promotion of friendship between the members. All of us, from time to time, have received help from our confrères by advice or the supply of information or material. On two occasions the Club has been responsible for the mass collection of material from the members, from which important conclusions were drawn and made public at an earlier date than would have been possible if all the data had been dependent upon one observer. We refer to Hay's paper upon the value of quinidine in the treatment of auricular fibrillation and to Gibson's paper upon ischaemic necrosis of the heart. It seems desirable that this procedure should be repeated as occasion demands.

Webb's egg has grown and the stripling is thriving. Under the new constitution we anticipate a strong and healthy adult life.

JOHN COWAN AND OTHERS

GENERAL MEETINGS OF THE CARDIAC CLUB

1922.	April 22.	Oxford	Chairman, A. G. Gibson
		Decision to form the Cardiac Club	
1922.	November 22.	University College Hospital, London	
		First General Meeting	„ Sir Thomas Lewis
1923.	May 17.	Edinburgh	„ W. T. Ritchie
1924.	June 5.	Bristol	„ Carey Coombs
1925.	May 28	Royal Soc. of Medi- cine, London	„ T. F. Cotton
1926.	May 20.	Newcastle	„ W. E. Hume
1927.	June 2.	Belfast	„ J. E. MacIlwaine
1928.	May 24.	Liverpool	„ John Hay
1929.	April 4.	Cambridge	„ A. N. Drury
1930.	June 5.	The London Hospi- tal, London	„ John Parkinson
1931.	May 21.	Manchester	„ Crighton Bramwell
1932.	May 12	Liverpool	„ John Hay
1933.	April 6.	Glasgow	„ G. A. Allan
1934.	May 7.	Leeds	„ Wardrop Griffith
1935.	June 6.	St. Thomas Hospital, London	„ Sir Maurice Cassidy
1936.	May 28.	Manchester	„ Crighton Bramwell
		Fifteenth and last General Meeting of the Cardiac Club.	
1937.	January 8.	An Extra-Ordinary Meeting was held at Guy's Hospital, London (Chairman, Bramwell) at which it was decided that the Cardiac Club should be trans- formed into the Cardiac Society of Great Britain and Ireland.	

MAIN SUBJECTS OF DISCUSSION

1922.	Infective Endocarditis	Sir Thomas Horder
1923.	The Use of Quinidine	Hay and Parkinson
	Abnormal QRST Complexes	MacIlwaine
1924.	The Heart in Pneumonia	Wardrop Griffith
	Digitalis	Fraser and Andrus (introduced).
	The Effect of Adrenalin on the Heart	Hume and Fraser
	Heart Disease in Children	Cotton and Carey Coombs
1925.	Anæmic Necrosis of the Heart	Gibson
	Simple Tachycardia	Parkinson
	Blood Pressure	Bramwell and Carey Coombs
	Cardiovascular Syphilis	Cotton
1926.	The Heart in Hypertension	Wilkinson
	Angina Pectoris	Starling
1927.	Heart Block	Kennedy
	Treatment of Œdema	Patterson
1928.	Angina Pectoris	Ritchie
	Injection of the Coronary Arteries	John Campbell (introduced)
1929.	Cardiac Asthma	Fraser and Emmanuel
	Vaso-vagal Attacks	Starling
1930.	Mitral Stenosis	Cowan
	The Heart and Athletics	Bramwell
1931.	Ætiology of Heart Disease	Carey Coombs
1932.	The Heart in Diphtheria	Hume and Wilkinson
	The Heart in Influenza	Herapath
	The Influence of Tobacco	Maurice Campbell
	The Influence of Alcohol	Patterson
1933.	Abnormalities of the T wave	Cowan and Allan
	Right and Left Ventricular Complexes	Drury
1934.	Diseases of the Pulmonary Artery	Parkinson and Bedford
	Vaso-motor Angina	Cassidy and Patterson
1935.	Heart Symptoms and Gall Bladder Disease	Cotton and Hume
	Cardiac Disease of Unknown Ætiology	Stott and Maurice Campbell
1936.	Heart Disease and Pregnancy	Bramwell
	Heart Block	Gilchrist

THE CARDIAC SOCIETY

After the meeting of the Cardiac Club in 1935 it was suggested that, with the increasing numbers who were interested in Cardiology, the time might have come for expanding into a larger and more representative society and that the Executive should consider this possibility.

At the 1936 meeting in Manchester a memorandum which had been drawn up by the Executive (Allan, Bedford, Drury and Wilkinson) provoked a long discussion. After general approval of the principle of expansion the following committee was appointed to draw up a scheme for submission to a special meeting of the club.

Members : Evan Bedford, Crichton Bramwell, F. R. Fraser, John Parkinson and Maurice Campbell (Secretary).

The committee held several meetings and drew up a draft constitution and rules for the Cardiac Society, and lists of names of those who should be invited to be Honorary, Extra-Ordinary, Ordinary and Associate members.

The last meeting of the Cardiac Club was a special one held in the Governor's Committee Room at Guy's Hospital on January 8, 1937. It was decided to accept these proposals for the formation of the new society, for its rules and constitution, and for the names of those who were invited to be the original members. The following were chosen as the first Council : Allan, Evan Bedford, Crichton Bramwell, Gilchrist (President 1937), Parkinson, Wilkinson and Maurice Campbell (Secretary and Treasurer).

At the First Annual Meeting of the Cardiac Society, held at Edinburgh on April 15, 1937, practically all the members attended, and in addition to the scientific business a committee was appointed to consider the possibility of starting a journal dealing with cardiology. *Members :* Gibson (Chairman), Evan Bedford, Maurice Campbell, Fraser and Wilkinson.

Several meetings were held, and in February 1938 the committee reported to the Council. They recommended that such a journal should be started and that the British Medical Association should be asked to publish it, as after various negotiations and meetings they thought that the British Medical Association were able and willing to publish a journal that would meet the needs of the Society. These recommendations were approved by the Council of the Cardiac Society, which appointed the Editors and the Editorial Board for the Journal. The title which has been chosen was suggested at an early stage, but many other titles have had their supporters. The action the Council had taken with reference to the Journal was approved by the Society at its Second Annual Meeting at Bristol on June 2, 1938.

MAURICE CAMPBELL,
Secretary of the Cardiac Society.

BRITISH HEART JOURNAL. EDITORIAL NOTE

For some time the need for a journal representative of British Cardiology has been apparent, and the Cardiac Society of Great Britain and Ireland, feeling assured of adequate support, has taken the initiative in starting the *British Heart Journal*. The Society's project has been facilitated by the generous co-operation of the British Medical Association, which has undertaken the responsibility of publishing and distributing the Journal.

To those who hold that specialization has already gone too far, the appearance of another journal devoted to a special branch of medicine may seem a step in the wrong direction. In Harvey's time medicine had no offspring, for the surgeon was no more than the servant of the physician. One by one, Anatomy, Physiology and Pathology began to develop independently of the parent science, and in the course of time further separation has occurred, to meet the exigencies of practice, teaching, and research.

But even traditional divisions in medicine are not inviolate, and already the barrier between Medicine and Surgery is yielding, for example in the fields of Neurology and of Diseases of the Lungs. Radiology has become a special branch of medicine on grounds of expedience alone, for it is no more than a method of examination, and incidentally one which is readily applicable to the heart. Cardio-vascular radiology has been and is being developed as a means of diagnosis by those interested in the heart, whether primarily physicians, radiologists, anatomists or physiologists. The special journal represents an attempt at reorientation; its proper function is to bridge the barriers separating existing divisions in medicine, and not to create new ones. By providing common ground on which physicians, anatomists, physiologists and pathologists may meet and pool their efforts in a particular direction, it enables those who treat the sick and those who work mainly in the laboratory to keep in contact with each others problems in the same field, to their mutual advantage.

The *British Heart Journal* will naturally reflect first and foremost the interests of members of the Cardiac Society, interests that are predominantly though not exclusively centred in the clinical aspects of cardio-vascular disease; but the policy of the Journal, and indeed of the Society, will be to serve all those interested in the Heart and Circulation, irrespective of their calling.

In starting the *British Heart Journal*, we are not unmindful of its predecessor, *Heart*, founded by Sir Thomas Lewis nearly thirty years ago. During the period when knowledge of electrocardiography was developing, *Heart* rendered invaluable service to Cardiology and maintained a standard and reputation second to none among the scientific journals of the world. In changing the title to *Clinical Science*, Sir Thomas Lewis has indicated his intention of widening its scope and thus increasing its field of usefulness to those engaged in research. The Cardiac Society are indebted to him for his generous co-operation, and we take this opportunity of thanking him for his support and for contributing a foreword.

D. EVAN BEDFORD.

THE NORMAL ELECTROCARDIOGRAM

BY

E. NOBLE CHAMBERLAIN AND J. DUNCAN HAY

From the Heart Department, the Royal Infirmary, Liverpool

Received November 18, 1938

It is necessary at intervals to revise our standards of the normal in all sciences. This is particularly desirable in electrocardiography, where important advances are made yearly in its application to the diagnosis of cardiac disease. It is very easy for minor changes in the electrocardiogram to loom too largely in the diagnostic picture ; but if the wide limits of normal variation are realized, some of the pitfalls will be avoided.

The most important early work on the normal electrocardiogram is that of Lewis (1912), who constructed tables giving the amplitude of various waves and the length of the various intervals usually measured in the human electrocardiogram. His work was carried out on fifty healthy subjects and the description of the characteristics of each wave forms the basis of our present-day interpretation of the electrocardiogram.

Another and more recent important contribution was the study of the electrocardiogram in late middle life by Jensen, Smith, and Cartwright (1931-2). Their investigation consisted of the analysis of fifty cases between the ages of fifty and sixty-five to determine if there were "any changes which, though not common in the tracings of younger people, could nevertheless be considered physiologic at this stage of life". Their conclusions are summarized below.

(1) The following findings were not considered pathological :

- (a) Diphasic or iso-electric P waves in lead I, or inverted P waves in lead III if they become upright on deep inspiration.
- (b) Slurring of the QRS complexes, especially in lead III, and slight to moderate notching of R, with the QRS interval below 0.10 sec.
- (c) " Transverse heart."
- (d) Isolated left ventricular preponderance.
- (e) Moderate inversion of T in lead III.

(2) The following findings, on the other hand, were not present in their series and were therefore to be looked upon with suspicion :

- (a) Indeterminate or inverted P waves in leads I or II.
- (b) Inverted P waves in lead III if they did not become upright on deep inspiration.
- (c) P-R interval exceeding 0.20 of a second, QRS interval exceeding 0.10, or S-T exceeding 0.34-0.36 of a second (the upper limit seems slightly uncertain).

They conclude that there did not seem to be any characteristic changes in the electrocardiogram with increasing age. The writers of the present paper felt that a larger series of cases might indicate whether some of the minor defects sometimes taken as pathological could, in reality, be physiological. At the same time it was hoped to make a more extensive study of the variation of the electrocardiogram with age.

CLINICAL MATERIAL

Each subject was, as far as possible, subjected to such a clinical examination as to exclude the likelihood of any cardiovascular disease or of any disease likely to affect the cardiovascular system temporarily. A large number were nurses and medical students apparently in perfect health. Others were patients in hospital for trivial surgical causes, and in them a generous interval was allowed after any operative interference had been undertaken. All cases that had any symptoms suggestive of cardiac involvement, any rise of blood pressure, any enlargement of the heart, or any murmurs which were not clearly functional were rigorously excluded. Further, no one who had suffered from rheumatic fever, chorea, repeated tonsillitis, syphilis, or other ætiological factors of heart disease was included. The Wassermann reaction was performed in each and the subject excluded if it was positive.

In all, 302 subjects were examined of whom more than half were in the third and fourth decades, a period of life when the cardiovascular system is likely to be intact. Measurements were made of the amplitude of P, Q, R, S, and T in all three leads. The time intervals P-R, QRS, and S-T were measured only in lead II. Details of these figures are to be seen in the accompanying tables.

RESULTS

The results may be summarized as regards the various waves, axis deviation, and the time intervals.

P Wave.—In a number of instances P 1 was flat or scarcely perceptible. P 2 was usually well developed, and P 3 variable. Inverted P waves of a well-defined character were only observed in lead III. Four examples were noted in the second, third, and fifth decades. Occasional splitting of the summit of the P wave was noticed, not unlike that found more frequently in mitral stenosis.



FIG. 1.—Types of P wave : (A) P with broad summit ; (B) Bifurcation of P ; (C) Absent P in lead I.

Q Wave.—Q was absent in a large number of cases and was never more than 4.5 mm. in amplitude.

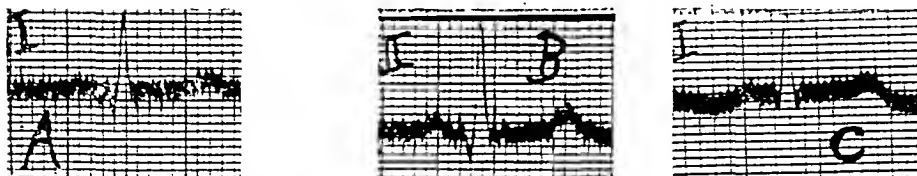


FIG. 2.—Types of Q wave : (A) and (B) Well-defined Q waves ; (C) Q scarcely perceptible.

R Wave.—The limits of variation in this wave were extreme. In lead I the wave might be as little as 1.5 mm. or as much as 18.6 mm. ; in lead II as little as 3.6 mm. or as much as 23.6 mm. ; whilst in lead III it varied between 0.5 and 20.5 mm. Slight notching of R was fairly common in all leads, especially in the descending limb. Splitting and low voltage of the QRS complex in lead III was very common.



FIG. 3.—Types of R wave : Three examples of slight degrees of notching of R in lead I.

S Wave.—This varied from 0.0 to 11.5 mm. and Fig. 4 shows well-defined waves. In many cases the descending limb of R did not come straight down to the iso-electric line, but sloped gradually into it (Fig. 5).

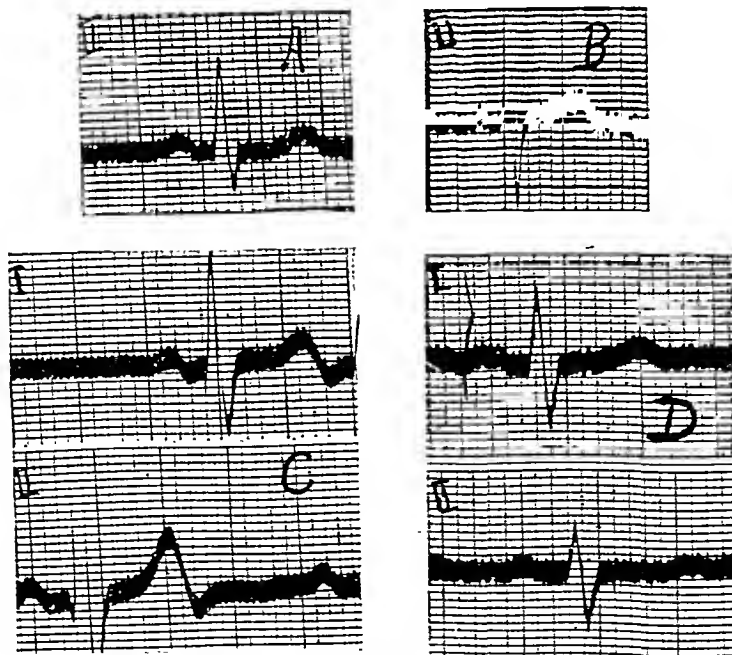


FIG. 4.—Types of S wave : (A) and (B) S well defined, prominent in B ; (C) and (D) S prominent leads I and II.

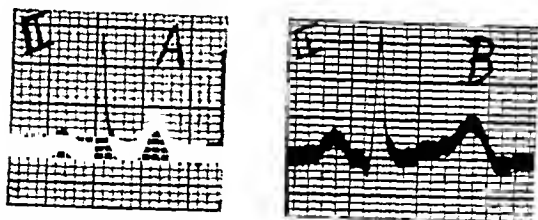


FIG. 5.—Types of S wave : (A) and (B) S indeterminate, slurring into R-T segment.

S-T Interval.—The S-T interval was studied with particular care in view of its great importance in relation to coronary thrombosis. Slurring of the R wave into the S-T segment was not uncommon (Fig. 2) especially when the portable electrocardiograph was used, and must also be distinguished from genuine S-T deviation. Out of 302 cases only 5 records showed the slightest S-T deviation. Occasionally there was a false impression of S-T deviation due to the fact that the P-Q interval sank below the iso-electric level. The degree of S-T deviation observed in the cases mentioned did not amount to more than 1.5 mm. (Fig. 6).

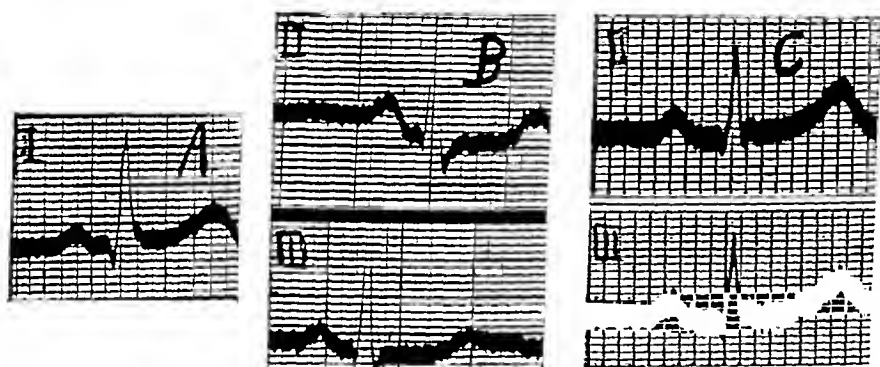


FIG. 6.—Types of S-T interval : (A) Slight S-T deviation ; (B) Slight S-T depression in leads II and III ; (C) False impression of S-T deviation owing to depression of P-Q interval.

The configuration of the S-T interval varied greatly in different normal subjects. In some there was a long iso-electric period often lasting 0.16 of a second, while in others it was shorter or absent (Fig. 7). In some cases where there was no iso-electric period, the T wave took origin in a steep fashion from a deep S wave (Fig. 8).

QRS Complex.—The QRS complex showed great variation in lead III. This fact is well established, and it is rare to find any pathological importance attached to it. A more careful study was made of the variation in leads I and II. Out of the 302 cases examined, only 15 showed any notching of the QRS in these leads (Fig. 9), and another 11 showed low voltage without notching (Fig. 10). Whenever notching was prominent some degree of low voltage was usually present.

Axis Deviation.—Right ventricular preponderance was noted in 3 cases in a pronounced form and to a slight degree in 15 others. Left ventricular

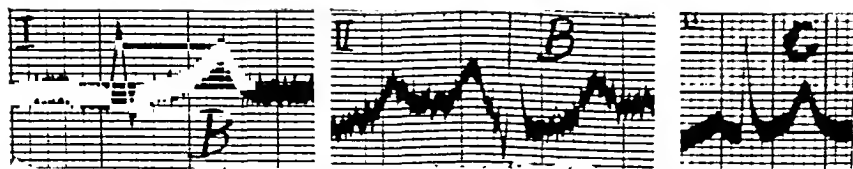
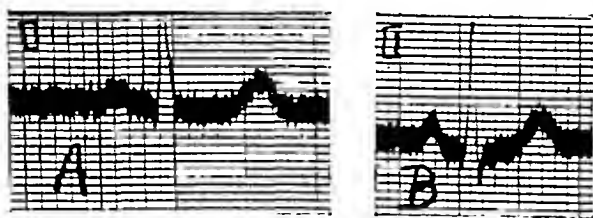


FIG. 7.—Type of S-T interval in leads I and II : (A) Long iso-electric period before T wave ; (B) Short iso-electric periods ; (C) No iso-electric period.

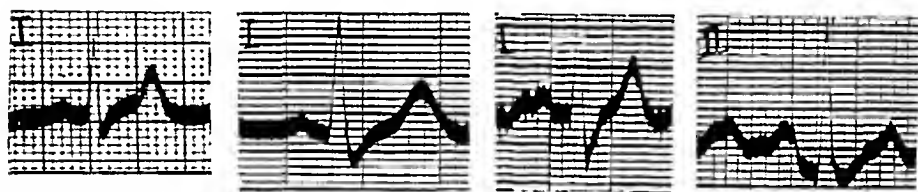


FIG. 8.—Types of S-T interval in leads I and II : Four cases showing no iso-electric period, T taking origin from a deep S wave.

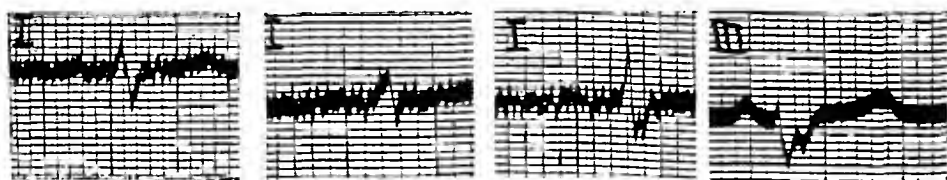


FIG. 9.—Types of QRS ; Notching : The first three cases show various types of notching of QRS in lead I ; the fourth shows pronounced notching of QRS in lead III.



FIG. 10.—Types of QRS ; Low voltage : Two examples of low voltage in lead I.

preponderance occurred in a moderate or pronounced form 26 times, i.e., in 8 per cent. of all cases; and slighter degrees were present in another 24 cases. In the third decade where 136 cases were available, there were 9 with slight and 7 with pronounced left ventricular preponderance, i.e. a total of 12 per cent. It would appear, therefore, that left axis deviation is a comparatively common finding in the normal electrocardiogram. It is notable that minor degrees of ventricular preponderance vary from complex to complex, probably due to respiratory variations.

T Wave.—The T wave varied greatly in amplitude, in the case of positive waves from 0.0 to 12.5 mm. The commonness of inversion of T 3 is universally recognized, but it is interesting to note that it occurred in as many as 87 out of 302 cases. In view of the attention paid to the various shapes of inverted T (e.g. in digitalis poisoning and coronary thrombosis) it is also important to recognize that considerable variation may be found in the normal from rounded waves to quite sharp ones (Fig. 11). In no case was inversion of T observed in lead I (although T was often flat), but inversion in leads II and III together was present in four cases.

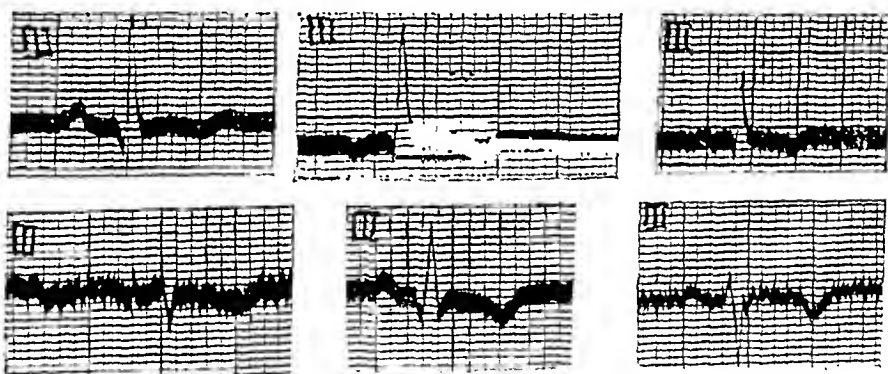


FIG. 11.—Types of negative T in lead III.

Time Intervals : P-R.—This interval varied from 0.12 to 0.22 of a second. The reading of 0.22 occurred in four subjects, three of whom were young people (Fig. 12). This is notable in view of the generally accepted view that the P-R interval should not exceed 0.20 of a second.

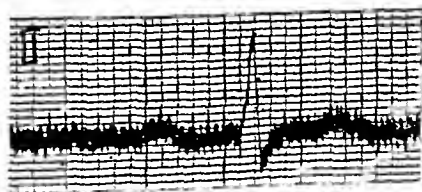


FIG. 12.—Prolonged P-R.: Four examples of a P-R interval of 0.22 of a second occurred in this series of 302 normal persons.

QRS.—The minimum was 0.04 seconds and the maximum 0.10, figures not varying from those usually accepted as normal.

S-T.—The minimum was 0.20 of a second, though such a low figure was only observed in a child. The maximum was 0.36 of a second.

DISCUSSION OF RESULTS

Table I has been constructed to compare the average measurements of the electrocardiogram in the second, third, and fourth decades with those in the fifth, sixth, and seventh. As Lewis's work was principally on young persons, it will be more satisfactory to compare his results with those of the second, third, and fourth decades.

A comparison indicates that, on the whole, there are no great differences between his figures and those of the present series, though in the latter the amplitude of most waves appears to be rather greater.

The P wave showed an average amplitude of 0.8 and 1.9 mm. in leads I and II, compared with figures of 0.52 and 1.16 mm. in Lewis's series. In both series P averaged 0.8 mm. in lead III.

The measurements of Q were almost identical in the two series. The measurements of R were uniformly greater in all three leads in the present series. S showed no appreciable difference, and T was only slightly greater in leads I and II.

TABLE I
COMPARISON OF AVERAGE MEASUREMENTS IN NORMAL SUBJECTS

Decade			P	Q	R	S	T
Lead I							
2nd, 3rd, and 4th	0.8	0.5	8.1	2.0	2.8
5th, 6th, and 7th	0.7	0.7	7.9	1.5	2.2
Lead II							
2nd, 3rd, and 4th	1.9	0.8	14.0	3.0	3.2
5th, 6th, and 7th	1.8	1.1	11.4	2.4	2.8
Lead III							
2nd, 3rd, and 4th	0.8	0.6	8.8	1.5	0.3
5th, 6th, and 7th	0.8	0.7	5.8	2.1	0.0

AGE VARIATIONS

The changes with age were less than might have been anticipated. There were no significant changes in the P waves in any leads.

The Q waves showed a slight increase in all leads in the aggregate of the fifth, sixth, and seventh decades.

The R waves in leads II and III appeared to be maximum in the third and fourth decades, but the amount of variation was not enough to be of any importance. On the whole, however, the later decades showed a rather smaller amplitude in the R waves than the earlier ones.

The S waves did not appear to be materially altered.

The T wave in lead I seemed to be larger in the earlier decades of life. In leads II and III it was also rather larger, though comparison of the average figures for the second, third, and fourth decades with the fifth, sixth, and seventh decades did not show any great difference.

Table II shows that there was no appreciable difference in the average P-R interval or in the duration of QRS or of S-T between the three earlier and the three later decades.

TABLE II

AVERAGE DURATION OF P-R, QRS, AND S-T IN LEAD II IN EARLIER AND LATER DECADES

		P-R	QRS	S-T
2nd, 3rd, and 4th decades ..		1.8	0.06	0.28
5th, 6th, and 7th decades		1.7	0.06	0.28

Left ventricular preponderance, as might be expected, was greater in the later decades of life. Out of 136 cases in the third decade it occurred in a pronounced form in 5 per cent., whilst out of 88 cases in the fifth, sixth, and seventh decades it occurred in 16 per cent. Those cases which showed inversion of T in leads II and III occurred in the third and fourth decades. The incidence of negative T waves in lead III was, curiously enough, greater in the first decade (6 cases), though the total number available in this decade was too small (8 cases) to draw any definite conclusions. Apart from this anomaly, the incidence of a negative T wave in lead III appeared to be roughly similar in all decades of life.

SUMMARY

1. To determine the limits of physiological variation in the electrocardiogram and any changes that might occur with age, 302 normal subjects have been investigated. Each was subjected to a rigorous examination, including blood pressure readings and Wassermann reaction. The following points are deemed worthy of emphasis.

2. The P wave was often flat or scarcely perceptible in lead I and occasionally had a split or broad summit. A few examples of inversion of P 3 were seen.

3. The R wave varied within wide limits in its amplitude and slight notching of the descending limb was not uncommon.

4. The S wave, although usually well defined, may slope gradually into the R-T segment.

5. True S-T deviation was so rare and so minute that it must be regarded with great suspicion, but peculiarities in the formation of the S-T interval were very common and must not be confused with genuine S-T deviation.

6. Slight degrees of notching and of low voltage in the QRS complex in leads I and II were not uncommon. The types of record found can be seen better by inspection of the illustrations than by description.

7. Right axis deviation in a pronounced form was uncommon even in young persons, whilst left axis deviation occurred quite frequently at all ages, increasingly so in the later decades where it was found in one sixth of all cases.

8. Inversion of T was never found in lead I, but inversion of T in both leads II and III was present in four cases. The former must be considered as pathological whenever it occurs, and the latter as suspicious. Inversion of T in lead III only was present in 29 per cent. of the total 302 cases and considerable variation in the shape of the wave was recognized.

9. The only unusual finding as regards time intervals was the occurrence of a few cases where the P-R interval was 0.22 of a second.

10. Age variations were slight, the most important being an increase in the left axis deviation in the later decades of life.

We wish to thank Dr. J. L. Chisnall for his help in the statistical part of this work and Mr. E. Caldwell for his careful work with the electrocardiograms.

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TABLE III

MEASUREMENTS OF P, Q, R, S, AND T WAVES IN NORMAL SUBJECTS

			P	Q	R	S	T
Lead I			First decade ; 8 cases				
Average	0.9	1.0	8.2	1.7	3.1
Maximum	1.6	3.6	11.6	7.6	4.6
Minimum	0.0	0.6	5.6	0.0	1.6
Lead II							
Average	1.5	0.5	12.5	1.7	2.2
Maximum	3.0	4.0	19.5	2.5	5.5
Minimum	0.5	0.0	7.5	0.5	0.5
Lead III							
Average	-0.2	0.4	4.1	0.8	-0.5
Maximum	1.5	3.5	10.5	1.5	1.5
Minimum	-0.5	0.0	1.5	0.5	-1.5

TABLE III—continued

MEASUREMENTS OF P, Q, R, S, AND T WAVES IN NORMAL SUBJECTS

			P	Q	R	S	T
Lead I			Second decade ; 25 cases				
Average	1.0	0.9	8.8	2.3	3.3
Maximum	2.5	3.5	18.6	8.0	4.5
Minimum	0.0	0.0	2.0	0.0	1.5
Lead II							
Average	1.7	1.1	11.8	2.6	3.0
Maximum	2.6	2.5	23.6	11.5	6.5
Minimum	0.5	0.0	6.6	0.0	1.6
Lead III							
Average	0.2	0.5	6.0	1.6	1.1
Maximum	2.5	4.5	14.4	8.5	3.5
Minimum	-4.4	0.0	1.5	1.5	-2.0
Lead I			Third decade ; 136 cases				
Average	0.6	0.4	9.0	1.6	3.1
Maximum	1.5	2.6	18.6	7.5	6.5
Minimum	0.0	0.0	2.5	0.0	1.1
Lead II							
Average	1.7	0.5	15.6	3.0	4.2
Maximum	2.7	2.5	23.5	10.6	12.5
Minimum	0.5	0.0	6.5	0.0	0.5
Lead III							
Average	0.7	0.5	9.3	1.5	-0.3
Maximum	2.5	3.6	20.5	8.5	6.5
Minimum	-3.5	0.0	1.5	0.0	-5.5
Lead I			Fourth decade ; 36 cases				
Average	0.8	0.1	6.4	2.2	2.1
Maximum	1.5	0.5	10.5	4.5	3.6
Minimum	0.0	0.0	2.0	0.5	1.5
Lead II							
Average	2.4	0.7	14.6	3.5	2.4
Maximum	5.0	1.5	18.5	8.5	6.6
Minimum	0.5	0.5	7.5	0.5	-3.5
Lead III							
Average	1.5	0.9	11.2	1.5	0.1
Maximum	3.0	3.0	18.5	8.6	4.6
Minimum	-0.5	0.0	4.5	1.5	-4.5
Lead I			Fifth decade ; 42 cases				
Average	1.0	0.1	7.5	1.9	2.5
Maximum	2.6	2.0	13.5	3.6	3.5
Minimum	0.5	0.0	2.6	0.0	0.6
Lead II							
Average	2.0	0.6	12.4	3.0	2.7
Maximum	2.6	2.6	16.4	5.0	4.6
Minimum	0.0	0.0	4.5	0.0	0.6
Lead III							
Average	1.0	0.4	6.8	2.2	0.0
Maximum	2.6	4.0	13.4	4.5	2.5
Minimum	-4.0	0.0	1.6	0.0	-5.0

TABLE III—*continued*

MEASUREMENTS OF P, Q, R, S, AND T WAVES IN NORMAL SUBJECTS

			P	Q	R	S	T
Sixth decade ; 33 cases							
Lead I							
Average	0.6	0.7	7.8	1.2	2.0
Maximum	1.5	2.5	13.6	6.5	3.5
Minimum	0.0	0.0	1.5	1.5	0.0
Lead II							
Average	1.9	1.3	11.3	2.3	3.0
Maximum	3.5	4.5	16.5	9.5	7.5
Minimum	0.5	0.0	5.5	1.5	0.5
Lead III							
Average	1.4	1.2	5.9	2.2	0.5
Maximum	3.0	4.5	14.6	10.5	4.5
Minimum	-1.5	0.0	0.0	1.5	-4.5
Seventh decade ; 13 cases							
Lead I							
Average	0.9	1.2	8.4	1.4	2.1
Maximum	1.5	2.5	13.6	2.5	3.5
Minimum	0.0	0.0	2.5	0.5	0.5
Lead II							
Average	1.5	1.5	10.4	2.0	2.8
Maximum	2.5	3.0	17.6	4.5	5.5
Minimum	0.5	0.0	3.6	0.0	1.5
Lead III							
Average	0.2	0.5	4.6	2.0	-0.7
Maximum	1.5	2.5	18.6	7.5	3.5
Minimum	-1.5	0.0	0.5	0.0	-4.5

TABLE IV
MEASUREMENTS OF P-R, QRS, AND S-T INTERVALS IN SECONDS, IN NORMAL SUBJECTS
(LEAD II ONLY)

				P-R	QRS	S-T
				First decade		
Average	0.14	0.05	0.25
Maximum	0.16	0.06	0.28
Minimum	0.12	0.04	0.20
				Second decade		
Average	0.16	0.06	0.28
Maximum	0.22	0.08	0.32
Minimum	0.14	0.04	0.24
				Third decade		
Average	0.19	0.06	0.29
Maximum	0.22	0.08	0.36
Minimum	0.14	0.04	0.24
				Fourth decade		
Average	0.18	0.06	0.28
Maximum	0.22	0.08	0.32
Minimum	0.14	0.04	0.24
				Fifth decade		
Average	0.18	0.05	0.29
Maximum	0.20	0.06	0.34
Minimum	0.14	0.04	0.24
				Sixth decade		
Average	0.17	0.06	0.28
Maximum	0.20	0.10	0.32
Minimum	0.14	0.04	0.22
				Seventh decade		
Average	0.17	0.06	0.28
Maximum	0.20	0.08	0.32
Minimum	0.14	0.04	0.24

PERSISTENT CONDUCTION DEFECTS FOLLOWING DIPHTHERIA

BY

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Whether diphtheria commonly causes any permanent cardiac damage has long been the subject of discussion; but it is generally accepted that the persistence of electrocardiographic changes of any serious significance is extremely rare (Alstead, 1933 ; Beer, 1936 ; Begg, 1937 ; Hoskin, 1926 ; Jones and White, 1927 ; and Thompson, Golden, and White, 1937). It is not uncommon for complete heart block and bundle branch block to develop during the course of severe diphtheria, usually during the second week (Alstead, 1932 ; Begg, 1937 ; Franck, 1935 ; Place, 1932 ; and Schwensen, 1922). The mortality amongst cases showing these changes is high, but if the patient survives there is usually a complete cardiac recovery.

Parkinson (1915) has described the case of a man, aged 22, who, on the twenty-second day of a severe attack of diphtheria, developed complete heart block. This lasted for eleven days, when auricular fibrillation supervened. At first the ventricular rate was slow (50 per minute), but later increased to 100–110 per minute. The fibrillation persisted for at least six months. Sprague and White (1927) have reported the case of a woman, aged 22, with complete heart block dating from diphtheria 19 years before. Read (1929) described a woman, aged 48, with complete heart block which, it was believed, dated from an attack of diphtheria at the age of 6; and Chamberlain and Alstead (1931) have published the details of a woman, aged 28, with complete heart block following diphtheria 18 years before. Butler and Levine (1930), investigating twenty cases with heart block of obscure origin, found a history of diphtheria in ten, whereas of 600 surgical cases studied as controls the incidence of a history of diphtheria was only six per cent. As a result of these observations it was suggested that diphtheria may predispose to the development of heart block in later life. However, Thompson, Golden, and White (1937) investigated ninety-one patients who had severe diphtheria 15 to 20 years previously, but found no evidence that diphtheria predisposed to the subsequent development of conduction defects.

In view of the rarity of persistent defects in cardiac conduction after recovery from diphtheria, the three following cases appear worthy of record. In two there was persistent complete heart block and in one persistent bundle branch block.

TWO CASES OF COMPLETE HEART BLOCK.

Case 1. J. H., female, aged 14. Reported previously (Perry, 1931).

On November 13, 1929, this patient was admitted to Ham Green Fever Hospital on the third day of a severe attack of diphtheria. There was extensive membrane and a "bull neck." She was given 40,000 units of anti-toxin. On November 19 the pulse dropped to 70 and on December 10 to 54-60 per minute. From this time until she was discharged on February 6, 1930, the pulse rate varied from 48-64. Palatal palsy necessitated nasal feeding for a time. Complete heart block was first demonstrated on September 30, 1930, and since that time there has been no change in the cardiac rhythm or in the physical signs.

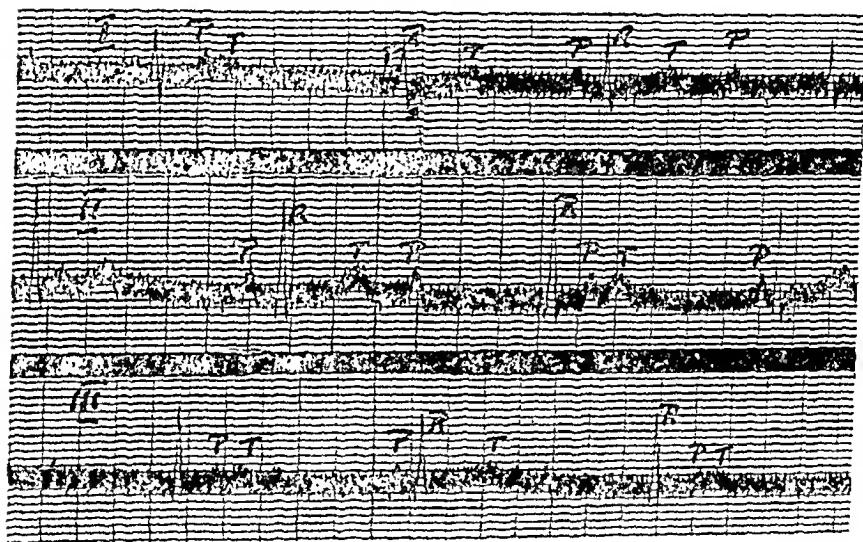


FIG. 1.—Electrocardiogram of Case 1.

She attends school normally, but is not allowed to take part in games or drill. There have been no symptoms referable to the cardiac lesion. The apex beat is diffuse and forcible in and beyond the mid-clavicular line. The heart sounds vary in intensity from beat to beat and there is an inconstant diastolic sound. There are no murmurs. The blood pressure is 115/70. An X-ray shows a heart which is generally enlarged, particularly the left ventricle, with a cardio-thoracic ratio of 65. An electrocardiogram shows complete heart block with a ventricular rate of 50.

Case 2. J. T., female, aged 13.

This patient was admitted to Ham Green Hospital on June 27, 1931, with very severe diphtheria which had commenced on June 23. There was extensive

membrane and œdema of the neck. She received 46,000 units of anti-toxin intravenously with five ounces of 20 per cent. glucose. At the end of the second week she showed the cardiac vomiting syndrome, which was treated by intravenous glucose and finally stopped. On July 8 palatal paralysis developed, followed on July 31 by strabismus and ptosis. After the second week the pulse remained between 80 and 90 until September 2, when it fell to 60. At the same time there was vomiting, pyrexia, and slight enlargement of the neck glands. The patient was discharged from hospital on September 18. On October 13 an electrocardiogram showed complete heart block. At that time there was some weakness of the leg muscles.

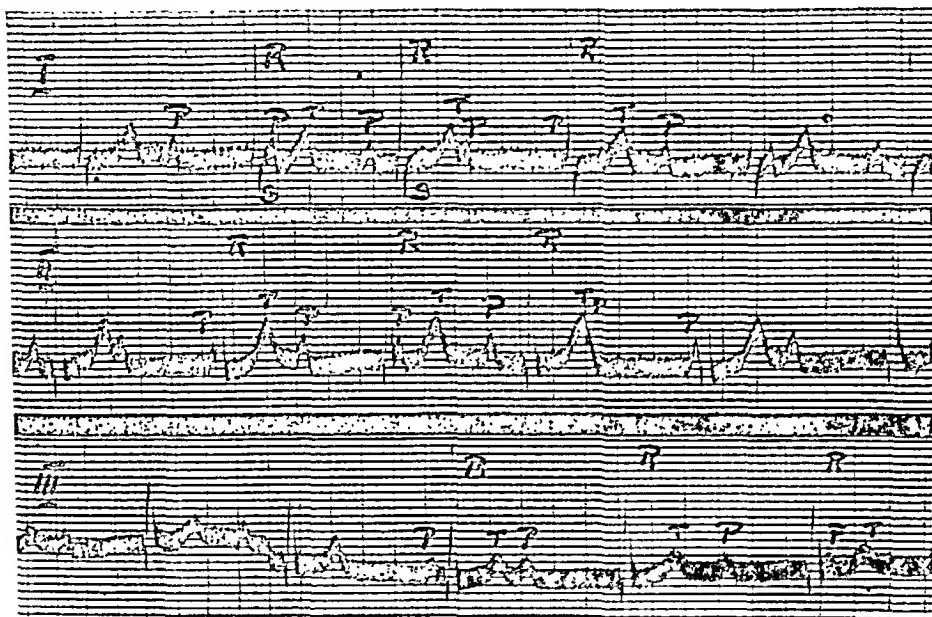


FIG. 2.—Electrocardiogram of Case 2.

By April 1932 she appeared to be perfectly well, but the cardiac condition was unchanged and has remained so ever since. She attends school normally, but is not allowed to take part in games or drill. The apex beat is diffuse and forcible beyond the mid-clavicular line. The heart sounds vary in intensity from beat to beat and there is an inconstant mid-diastolic sound. There is a loud apical systolic murmur. The blood pressure is 120/65. An X-ray shows an enlarged left ventricle with a cardio-thoracic ratio of 56, and a prominent pulmonary artery. The electrocardiogram shows complete heart block with a ventricular rate of 59.

Comment.

In these two cases of persistent heart block the conduction defect dates from an attack of severe diphtheria. In the first the heart block developed at the

usual time, during the second week of the illness. The very late development of the conduction defect in the second, associated with an apparent relapse or fresh infection forty days after the onset of the disease, suggests that the heart block may possibly be due to an attack of rheumatic carditis, and the apical systolic murmur may be considered further evidence of this. However, no other manifestations of acute rheumatism were noted and there has been no rheumatic episode since the heart block was discovered, such as might have been expected had this been rheumatic in origin. Alstead (1932) found that in the acute stage of diphtheria complete heart block might easily pass unnoticed without electrocardiographic studies, since the ventricular rate may be as high as 100 per minute. In view of this it is possible that the heart block in the second case developed before September 2, but this seems rather unlikely since there was a definite setback at the time with pyrexia and vomiting, quite apart from the fall in pulse rate.

A feature of both cases is the comparatively rapid ventricular rate. A similar rate has been noted in children with complete heart block due to rheumatic heart disease (Perry, 1931). It is interesting to note that in the cases of diphtheritic heart block described by Chamberlain and Alstead (1931) and by Read (1929) the pulse rates were both over 40 at the age of 28 and 48 respectively. It is curious that these two cases and the three reported by Sprague and White, by Chamberlain and Alstead, and by Read are all females.

ONE CASE OF BUNDLE BRANCH BLOCK.

Case 3. G. H., male, aged 16.

This boy was admitted to Ham Green Hospital on January 10, 1931, on the third day of a severe attack of diphtheria with extensive membrane and œdema

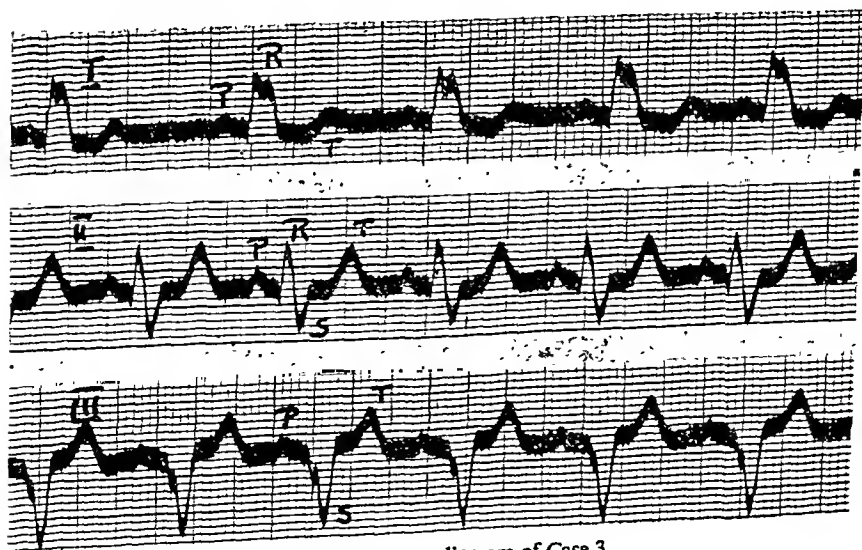


FIG. 3.—Electrocardiogram of Case 3

of the neck. He received 40,000 units of anti-toxin intravenously. On January 18 he developed palatal paralysis. On February 3 he vomited, the heart was dilated, and the liver was enlarged and tender. He was treated by intravenous glucose and improved. The heart remained dilated and the pulse rate 104-112 until April 29, when he was discharged from hospital at the parents' request.

On March 16, 1932, he was quite well and had no symptoms. The apex beat and heart sounds were normal and there were no murmurs. An electrocardiogram showed bundle branch block of the common (left) variety; this has been present whenever he has been examined since. At times a soft apical systolic murmur has been noted, but this is not constant. The blood pressure was 110/65. An X-ray showed a small vertical heart with a cardio-thoracic ratio of 45. He attended school normally, but was not allowed to play games or to do drill. He is now (1938) working quite successfully.

Comment

This last patient obviously suffered from very severe cardiac damage during the attack of diphtheria, and it would appear justifiable to attribute the persistent bundle branch block to this, since there has been no suggestion of any rheumatic infection before or after. This would seem to be the first record of a case of bundle branch block due to diphtheria that has persisted with the recovery of the patient.

SUMMARY

A description has been given of three children who recovered from attacks of diphtheria with persistent conduction defects. In two this took the form of complete heart block and in the third of bundle branch block. In all three the lesion seems to have developed at the time of their diphtheria or shortly after, and in all it has persisted for some years.

I am greatly indebted to Dr. B. A. Peters for very kindly supplying the information about these cases while they were in the Fever Hospital.

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PAROXYSMAL TACHYCARDIA ; ÆTIOLOGY AND PROGNOSIS OF ONE HUNDRED CASES

BY

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The early papers on paroxysmal tachycardia gave its essential features with great accuracy, and the modern reader will enjoy their lucid descriptions. After the classic account by Cotton (1867) with pulse tracings by the great Burdon-Sanderson, many cases were reported, and Bristowe (1887) and Bouveret (1889) collected these and added more of their own. Bristowe's paper was "On recurrent palpitations of extreme rapidity in persons otherwise apparently healthy" and Bouveret first introduced the modern name in "De la Tachycardie essentielle paroxystique"; he stressed that it did not produce organic heart disease, but thought it a serious malady, and as he recorded a fatal outcome in many of the longer attacks he may be responsible for the guarded prognosis often given in books. A few of these attacks were perhaps paroxysmal flutter, but with this exception the papers just quoted might still be read as accurate accounts of much of our clinical knowledge. Herringham (1897) emphasized that paroxysms often started in childhood and that the patient lived to a good age. Hoffmann (1900) wrote a book analysing 135 reported cases.

For some time little more was added, till the electrocardiogram made our knowledge more precise and enabled us to distinguish paroxysmal auricular flutter and to differentiate the various types of paroxysmal tachycardia. Hume (1930) has reviewed the whole subject, giving a full list of references, and for this reason most papers are only referred to here in connection with special points as they arise. Many of the large number of recent papers deal with the electrocardiographic features of single cases and pay less attention to the clinical picture of paroxysmal tachycardia as a whole.

This paper is based on observations on one hundred cases seen during the years 1925-32. A few with no features of special interest may have escaped indexing, but they were not many, and otherwise it is an unselected series. Cardiograms * of the paroxysms were obtained in 42; 30 others were seen by

* A good short word has not yet been coined for electrocardiogram, which is wasteful of time and space now it is in such constant use; no confusion is likely to arise by the substitution of the word cardiogram.

a doctor (occasionally by one of us) in the attack, though no graphic record was obtained ; and in 28 the diagnosis was made on the history alone. The occurrence of paroxysms in five students at Guy's Hospital during the years 1928-30 suggested that the condition was not uncommon, but only two more have been seen in the subsequent seven years.

Many of these patients have been followed over a long period, and as the immediate prognosis is nearly always good, this is essential for any complete picture. We have followed 16 until their death, not always from heart disease ; 53 have been seen or have replied fully to letters in 1937-38 and most of these and another 13 were seen in 1934-35, and we have no reason to expect any great change in their condition. The remaining 18 were last seen during 1925-32 and generally attacks had already occurred for some years. The series is therefore likely to give a fair view of those cases severe enough to come under medical observation, and has been followed long enough to give some approximation to a correct prognosis.

DIAGNOSIS

Often the attack is not seen and there is only the history ; this applied to 28 of our patients. Reliance must then be placed on the abrupt onset, and as a rule on the equally abrupt end. The rapid beating of the heart is nearly always the first symptom felt, whatever others may follow. If the patient is able to define the number of attacks and their duration it is almost diagnostic, since ordinary palpitation is much more vague and indefinite in its character. Enquiry must then be made as to whether the heart was regular or irregular, and, perhaps surprisingly, the patient's statement usually proves to be reliable, and only one had to be excluded from this series when a subsequent record showed it to be paroxysmal fibrillation. This suddenness of onset is the most reliable single symptom for diagnosis—"As if the pendulum of a clock had suddenly lost its weight" in the words of one patient. During the attack the heart action is a constant steady fluttering, and this word is often used.

The end of the attack is usually as sudden as the onset, but when the heart is diseased the patient may often be incapable of saying exactly when the end came. "I think it ended a few minutes ago, but it is still going very fast" was one description. This is specially so when the heart muscle is becoming worse, and in one such observation the rate appeared to fall gradually from 180 to 100 in the course of three hours, simple tachycardia having followed the paroxysm so that the exact ending was difficult to detect clinically : the offset is therefore less reliable than the onset. Most other symptoms are too variable to be reliable, and extrasystoles before or after the attack may obscure the clear picture.

When the attack is seen the diagnosis rarely remains doubtful, though it may not be thought of if the heart rate is 140 or less. It is sometimes difficult to distinguish paroxysms of tachycardia from those of flutter if a constant degree of heart block makes the ventricular rate regular, and impossible if the diagnosis has to be made on the history alone. The auricular rate in flutter is

generally 240–360; 4 : 1 heart block is rare in an untreated patient, and regular 3 : 1 heart block extremely rare; but 2 : 1 heart block is common and gives a rate of 120–180, i.e. within the usual limits of paroxysmal tachycardia. Again, flutter with the auricle at a slow rate without heart block (220–240) may be difficult or impossible to distinguish from paroxysmal tachycardia even on the cardiogram, and the decision may have to be made on clinical grounds. Lastly, a paroxysm of tachycardia may fall above its usual limits of 240 (Fig. 1).

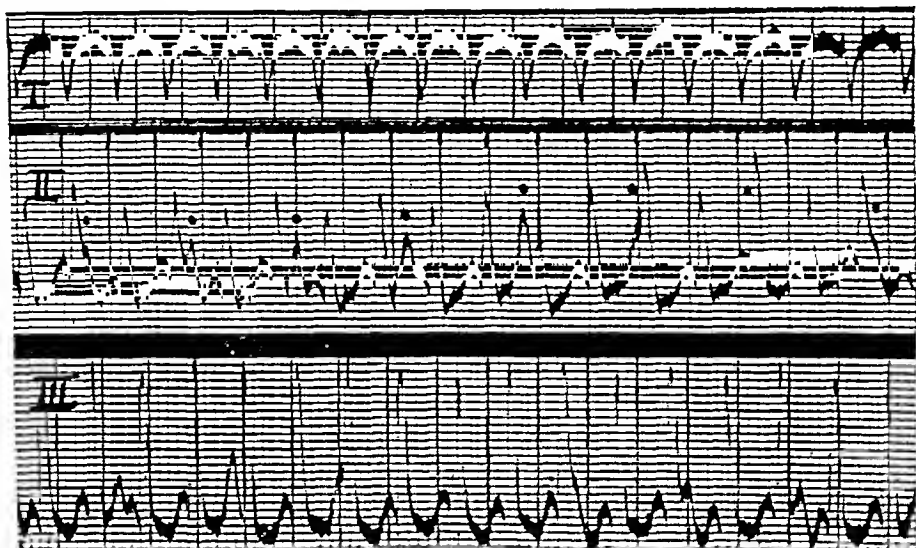


FIG. 1.—Ventricular tachycardia, auricle 128, ventricle 274; from a boy whose heart was otherwise normal (Case 69). The auricular waves have been marked with a *a* in lead II. The time marker in this and subsequent records indicates fifths and twenty-fifths of a second.

Apart from the rate, the following points may help to distinguish between paroxysmal flutter and tachycardia. If the regular rhythm is occasionally interrupted by a slower or irregular rhythm; if the rate can be halved by pressure on the neck; or if in the longer attacks the rate can be halved or made irregular with digitalis, the attack is flutter. Flutter, like fibrillation, is more often established than paroxysmal, but Parkinson and Bedford (1927) found that nearly one quarter of their cases of flutter had the paroxysmal form. Paroxysmal tachycardia very rarely lasts more than ten days and generally not more than four days: therefore the longer an attack of unknown origin lasts, the more likely it is to be flutter, and after ten days this becomes more certain. If the patient has high blood pressure or arteriosclerosis or if congestive failure develops rapidly, flutter must be thought of but cannot be diagnosed merely on these grounds. Occasionally even when a cardiogram is obtained there may still be difficulties, e.g. slow flutter without heart block, or a faster rate with 2 : 1 heart block where the P and T waves cannot be clearly distinguished.

TYPES OF PAROXYSMAL TACHYCARDIA

Every effort should be made to obtain a cardiogram of an attack ; not only to differentiate flutter, but to decide the variety of paroxysmal tachycardia, which cannot be determined in any other way and is of value in prognosis. It may still be difficult or impossible to subdivide the supraventricular into the various types of auricular and nodal, but fortunately this seems of less practical importance.

Of the 42 paroxysms recorded, 8 were ventricular. In three it was possible to identify P, occurring regularly at a slower rate than the ventricular complexes and quite unrelated to them, and so to prove that the paroxysms were ventricular ; the auricular rates were 150, 130, and 100, and the ventricular 220, 272, and 166 respectively (Fig. 1). In the remaining five ventricular records it was not possible to identify P, or there was retrograde conduction from the ventricle (Fig. 2). The type shown in Fig. 2 of very short paroxysms,

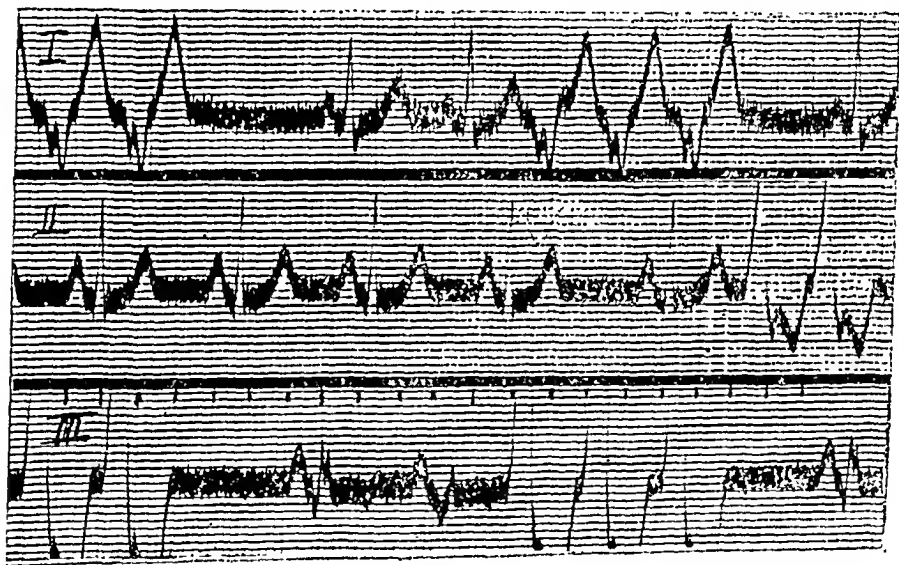


FIG. 2.—Short paroxysms of ventricular tachycardia, rate 142, probably with retrograde conduction ; from a young woman whose heart was otherwise normal (Case 34). This type may occur for years, apparently with little significance.

recurring frequently, may be found with a normal heart and seems to be of no serious significance even though it is ventricular.

If the QRS wave in the paroxysm was not widened or grossly aberrant, the focus was counted supraventricular. If QRS was widened and aberrant, it was compared with the QRS in the free intervals, and if different in conformation we considered the focus ventricular. Fig. 3 is an example we have called ventricular (though the P waves could not be seen) because the ventricular complexes of the attack differ from those of normal rhythm. This evidence is not conclusive, for the paroxysm may sometimes be auricular with aberrant

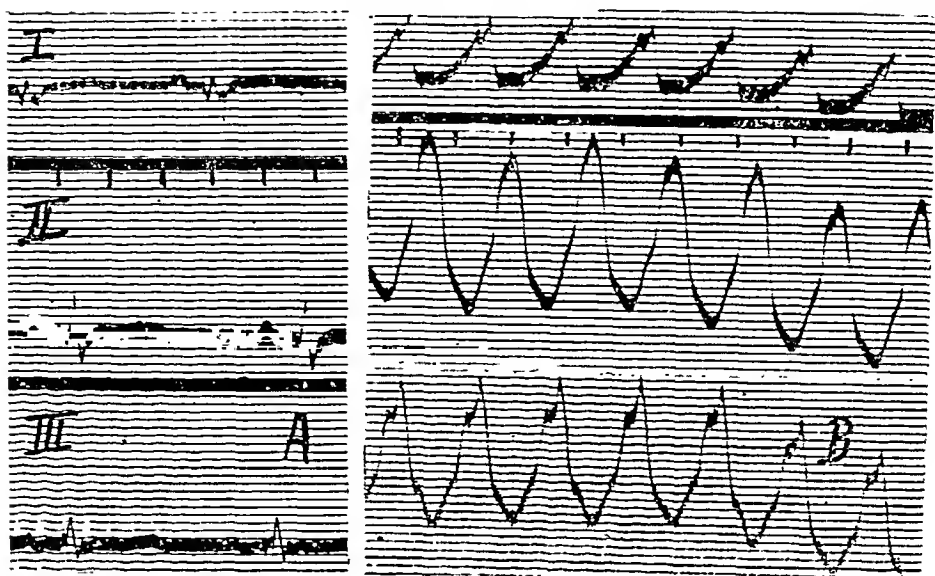


FIG. 3.—(A) Normal rhythm, and, (B) two days later, ventricular tachycardia, rate 207; there is no clear evidence of auricular activity but a suggestion of possible P waves, low on each second ventricular downstroke in lead III (Case 5).

conduction to the ventricle. If, on the other hand, QRS in the free interval was similar to that in the attack, we considered the focus as supraventricular. Such a paroxysm is shown in Fig. 4; it appears ventricular, but the QRS

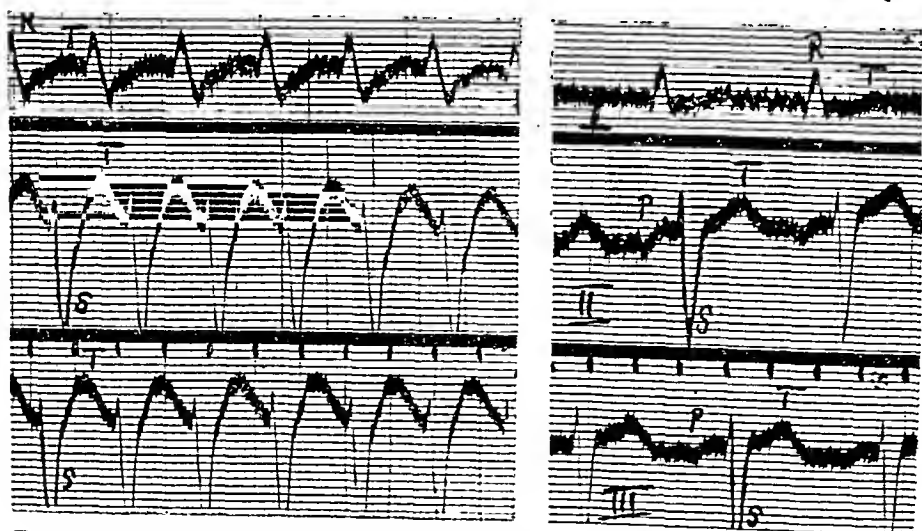


FIG. 4.—Supraventricular tachycardia, rate 175, simulating ventricular tachycardia because of the permanent defect of conduction: and normal rhythm; both from an elderly man with myocardial disease (Case 38).

complexes in the free intervals and in the attacks are identical; further, ventricular extrasystoles during normal rhythm did not resemble the ventricular waves of the paroxysm.

Levine (1927-28) has drawn attention to the slight irregularity in the rate and sounds in some ventricular paroxysms which may suggest the diagnosis on clinical grounds alone. On measuring the cardiograms this irregularity was present in two of our cases, but too slight to be appreciable to the finger or ear. Any gross irregularity is likely to indicate paroxysmal flutter with changing degrees of block.

Paroxysms of nodal tachycardia can usually be differentiated, but in many supraventricular paroxysms the exact site of origin cannot be defined. An example of auricular paroxysmal tachycardia is shown in Fig. 5. On the

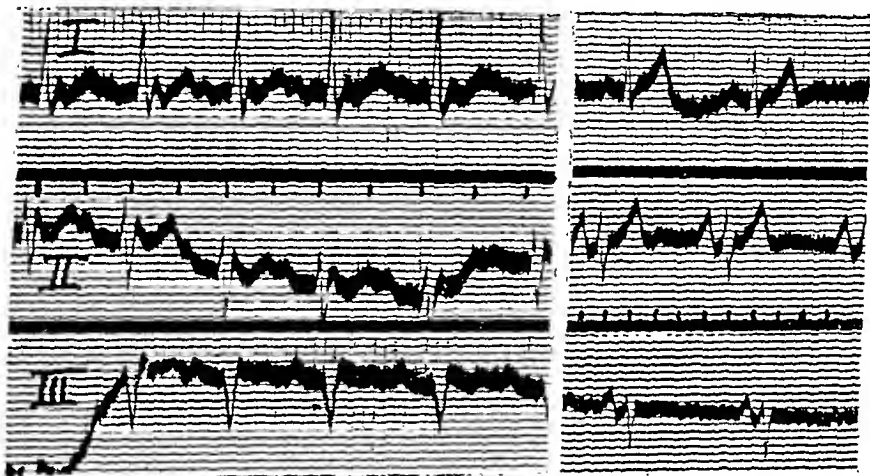


FIG. 5.—Auricular tachycardia, rate 142, simulating simple tachycardia: and normal rhythm; both from an elderly man whose heart was otherwise normal (Case 98).

picture alone it could not be distinguished from simple tachycardia; if the rate were a little faster P would be hidden in T, and one could not decide if it was an auricular attack with P hidden in T, or a nodal attack with P hidden in QRS. This seems to be a common difficulty when the beginning or ending of the attack is not seen (Figs. 9, 10).

Inversion of P indicates an abnormal focus in or near the A-V node, and its relation to QRS—whether before it with a short P-R interval, incorporated with it, or following it—indicates the level in the node of such focus. In two patients where the position and conformation of the P wave showed that the attack was nodal, it was inverted and preceded the QRS with a P-R interval that was normal (Fig. 6); this is sometimes described as superior or high nodal. In three more it was just before or with the QRS and was located by its large size (Fig. 7) or by recording a complete attack (Fig. 15a). This nodal group is relatively large in some published series and evidently includes many that we have left unclassified. The P wave was inverted and followed QRS in eight (Fig. 8), and these have been grouped as inferior or low nodal. In 13 of our 34 supraventricular cases there was no doubt of their nodal origin, two being high nodal, three nodal, and eight low nodal, and another three were

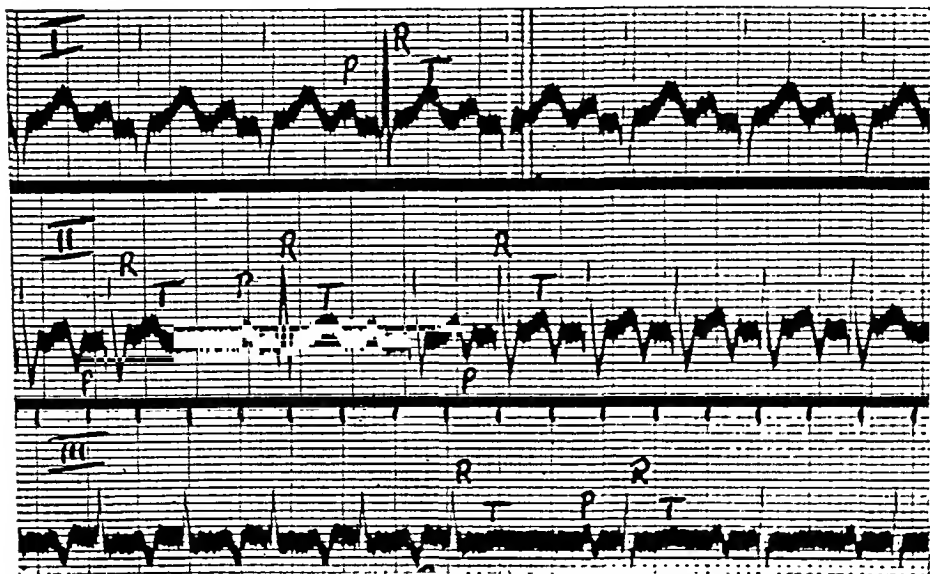


FIG. 6.—Nodal tachycardia of the "high nodal" type, rate 169, with the rhythm constantly changing ; from a boy whose heart was otherwise normal (Case 2).

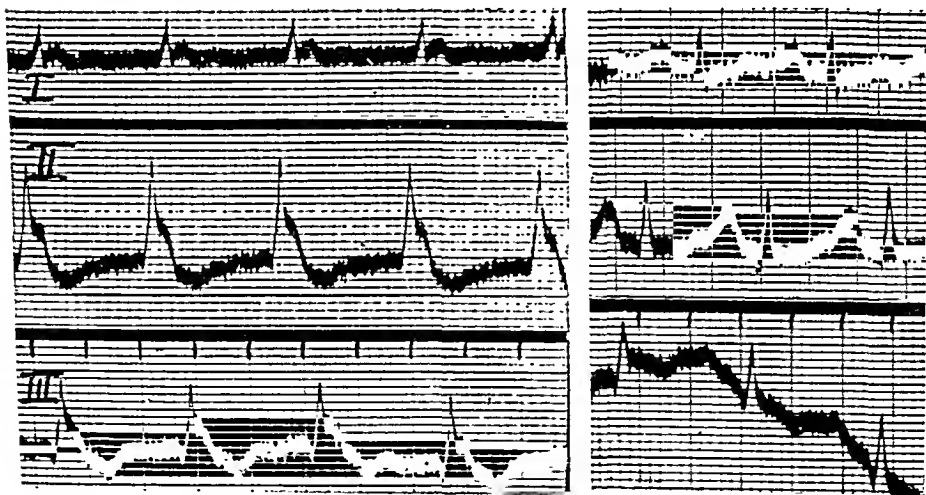


FIG. 7.—Nodal tachycardia of "intermediate" type, rate 125; and normal rhythm ; both from a woman with mitral stenosis (Case 87). The large P wave is incorporated with QRS on the downstroke of R.

probably nodal. This left 21 other supraventricular ; three were auricular but in the others there were no clear indications of the type (Figs. 9, 10).

Ritchie (1926) reviewed 138 cases, adding 14 of his own, and found one-third were ventricular. Hume (1930) collected the classification from various series as follows : auricular 40 ; superior nodal 8 ; inferior nodal 18 ; nodal 100 ; unclassified supraventricular 32 ; ventricular 55. But this is merely a

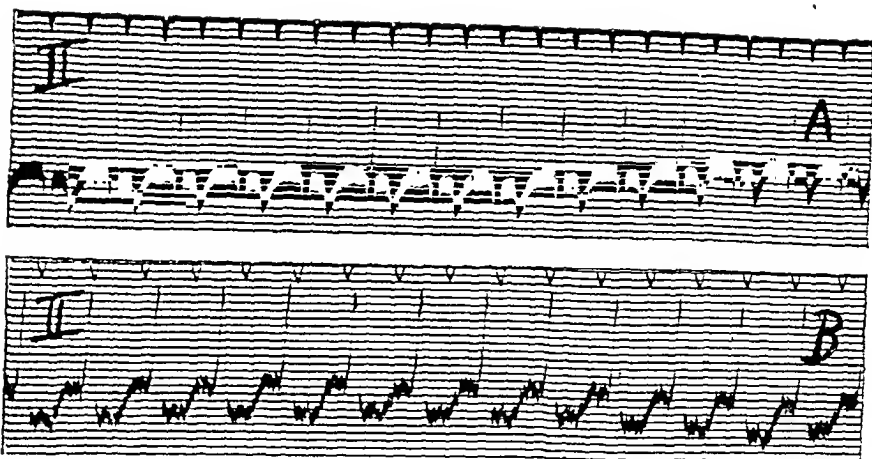


FIG. 8.—Nodal tachycardia of "low nodal" type, lead II only : (A) from a woman with mitral stenosis, rate 171 (Case 52) ; (B) from a woman with rheumatic aortic incompetence, rate 234 (Case 70).

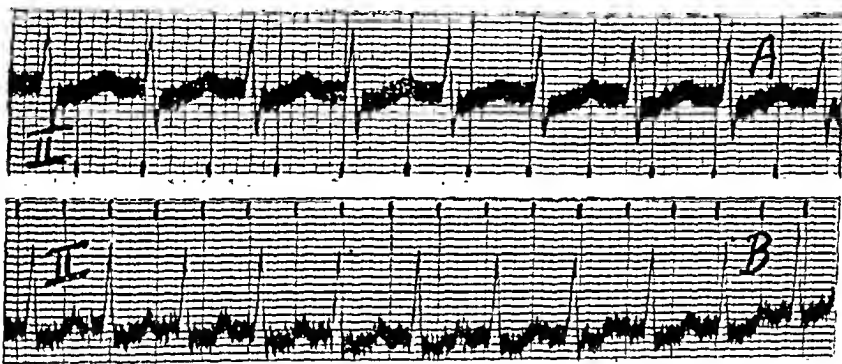


FIG. 9.—Supraventricular tachycardia, from two women with mitral stenosis : (A) rate 199 (Case 36) ; (B) rate 185 (Case 60).

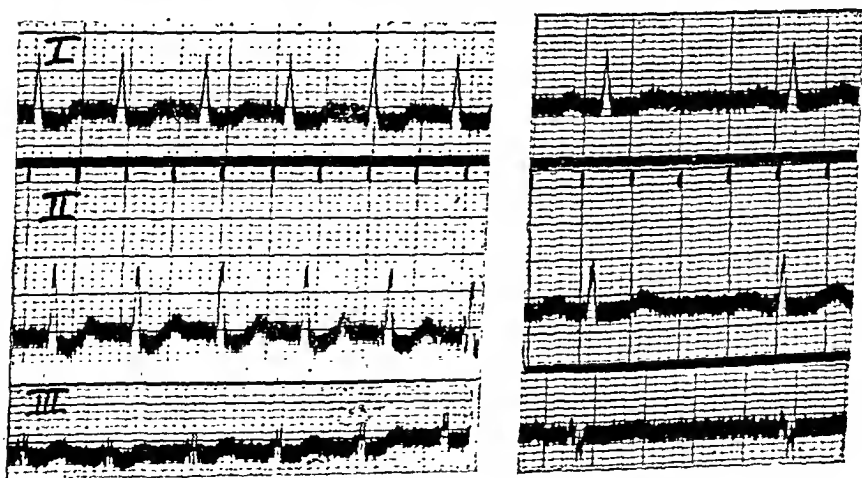


FIG. 10.—Supraventricular tachycardia, rate 172 : and normal rhythm ; both from an elderly man whose heart was otherwise normal (Case 58).

summary of some very discordant series, and we think that many classed as auricular or nodal should be left as unclassified supraventricular. The proportion of ventricular attacks in these series of Hume and Ritchie is in our opinion much higher than is an unselected series. Ventricular paroxysms occur most often in patients admitted to hospital for heart disease or even for failure, and so tend to be observed and reported ; many of these patients have been treated with digitalis and have had advanced heart disease ; and the paroxysms have occurred under these conditions on a few occasions, rather than periodically over a long time as with ordinary paroxysmal tachycardia. As instances, three of the five attacks reported by Gilchrist (1925-26) were almost terminal, and of the 65 patients reported by Strauss (1930) more than half were under treatment with digitalis for their heart failure and four-fifths had died within three months.

TABLE I

THE CORRELATION OF TYPES OF EXTRASYSTOLES AND OF PAROXYSMAL TACHYCARDIA

Type of Paroxysmal Tachycardia	Type of Extrasystoles recorded in the free intervals		
	Supraventricular only	Supraventricular and ventricular	Ventricular only
Supraventricular (34 cases)	5	5	2
Ventricular (8 cases) ..	0	0	4

It is said that the type of extrasystole observed in the free intervals will indicate the type of paroxysm and that extrasystoles are frequently observed in most cases of paroxysmal tachycardia. Often, however, this is not so, and as an example, in one patient seen each few weeks for ten years no extrasystoles have been noted. They were recorded in 16 of the 42 with records of their paroxysms (see Table I). Where supraventricular extrasystoles were observed (whether alone or with ventricular extrasystoles) the paroxysms were always of the supraventricular type, though auricular or nodal extrasystoles did not always indicate that the paroxysms were from the same focus. But where ventricular extrasystoles were observed the converse did not hold true : if they were the only type observed the paroxysms might be ventricular or supraventricular, though more likely to be the former ; but if they were of both types the paroxysms were always supraventricular.

ÆTIOLOGY

The first question to decide in each patient with paroxysmal tachycardia is whether there is any organic heart disease. This is essential for prognosis, and even slight signs may be very important. The ætiology of our hundred cases is shown in Table II, and rather more than half had no evidence of heart disease. The inclusion of those where there was no graphic record of the attack does not invalidate these conclusions about the ætiology ; the only

difference was that fewer records were obtained of the normals because they had less reason for attending hospital regularly.

TABLE II
ÆTIOLOGY OF 100 CASES OF PAROXYSMAL TACHYCARDIA

Ætiological Group	Number of Cases			
	Males	Females	Total	Number with Cardiogram during Attack
Normal	34	21	55	18
Rheumatic	4	15	19	13
Syphilitic	2	0	2	1
Hyperpietic	3	5	8	2
Thyro-toxic	0	4	4	1
Myocardial	9	3	12	7
Total	52	48	100	42

Men and women were equally affected, as the excess of women in the rheumatic group was balanced by the men in the myocardial and normal groups. The age incidence—the age at which the attacks started—is shown in Table III and Figure 11. In 11 per cent. they started before the patient was

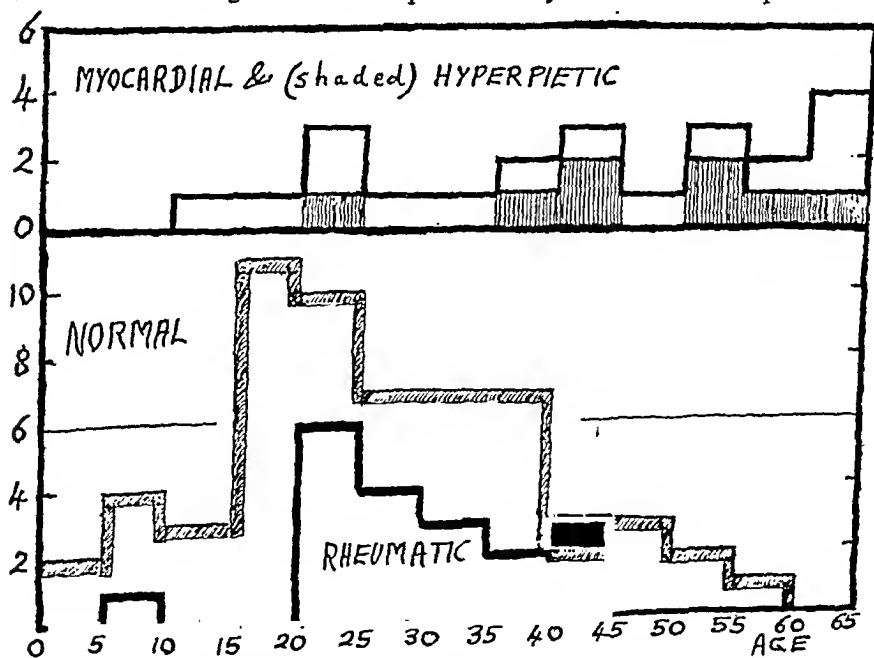


FIG. 11.—Diagram showing the age incidence at onset of paroxysmal tachycardia.

Above : 1. Hyperpietic and myocardial groups combined ; the hyperpietic are shaded and are mostly between 35 and 65, the myocardial are more evenly spread at all ages.
Below : 2. Normal group, at all ages with the main incidence between 15 and 40.
3. Rheumatic group, with the main incidence between 20 and 45 years of age.

fifteen, in 65 per cent. between fifteen and thirty-nine, and in another 12 per cent. before fifty, making 88 per cent. where the attacks started before this age.

TABLE III
AGE INCIDENCE AT ONSET OF PAROXYSMS

Age— in years	Number of Cases in each Group				Total
	Normal	Rheumatic	Hyperpietic	Myocardial	
0-4	2	—	—	—	2
5-9	4	1	—	—	5
10-14	3	—	—	1	4
15-19	11	—	—	1	12
20-24	10	6	1	2	19
25-29	7	4	—	1	12
30-34	7	3	—	1	11
35-39	7	2	1	1	11
40-44	2	3	2	1	7
45-49	3	—	—	1	5
50-54	2	—	2	1	5
55-59	1	—	1	1	3
60-	—	—	1	3	4
All ages ..	59*	19	8	14	100

* Includes 4 with goitre.

Most were hospital patients, and in those seen in practice since completing this series there have been fewer in the rheumatic group and more elderly patients with myocardial and coronary disease. They have been classified in the following six groups.

1. *Rheumatic Group* : 19 cases.—In all but one of these the attacks started between 20 and 44 years of age. There was valvular disease in 17, 10 with mitral, 5 with mitral and aortic, and 2 with aortic lesions ; the other 2 had a rheumatic history only.

2. *Syphilitic Group* : 2 cases.—Both had aortic incompetence ; and the paroxysms did not seem to influence the natural course of their disease. As there were no special features they have been included in the myocardial group for the tables, etc.

3. *Hyperpietic Group* : 8 cases.—Five of these, with an average age of 62 and an average blood pressure 180/105, may be taken as typical of the group. Their attacks were of relatively recent onset. Two elderly men were included, but probably the raised pressure was incidental, as their attacks had been present for 15 and 20 years ; two were not included, as paroxysms had occurred for 40 years. The eighth was unusual, as her attacks and high blood pressure both started after the removal of cystic ovaries. A less strict standard might have added one or two to this group, but among the normals there were very few who were even on the borderline.

4. *Myocardial Group* : 12 cases.—In many ways this was the most important group, though rather mixed. It comprised all those with heart disease who

could not be included elsewhere. Generally the signs were unmistakable, but occasionally even in young people the course of events showed serious heart disease with the paroxysms as the only early symptom, with a slight cardiac enlargement and/or an abnormal cardiogram as the only sign. They are discussed in more detail in the section on prognosis.

5. *Thyrotoxic Group* : 4 cases.—All were women with a goitre, but none had clinical hyperthyroidism. All have done well, and as they had no heart disease are included for subsequent discussion with the normal group. It is surprising that toxic goitre should be so much more frequently the cause of paroxysmal fibrillation (15 per cent. ; Parkinson and Campbell, 1930) than of paroxysmal tachycardia.

6. *Normal Group* : 55 cases.—The presence of paroxysms is not evidence that there is organic heart disease, and this group includes all those with hearts that were thought to be normal except for the paroxysms. Examples are given in the section on prognosis (see p. 149) of paroxysms for twenty or even sixty years without demonstrable heart disease at the end. Possibly a few have been wrongly included, but it seems certain that this group is much the largest. Details of the age when the attacks started are given in Table III. Naturally in this group the patients were younger, and nineteen were under 20, fifteen from 20–29, and twelve from 30–39, leaving only seven over this age and only three over 50 ; 72 per cent. were between 15 and 39 years of age at the onset of their attacks.

The ætiology of the 42 with records of the paroxysms are shown in Table IV. The only points of interest are the rarity of ventricular attacks in the normal and rheumatic groups, and that just over half of the nodal attacks were found in the rheumatic group.

TABLE IV
TYPE OF PAROXYSMS IN DIFFERENT ÆTIOLOGICAL GROUPS

Type of Paroxysms	Ætiological Group				Total
	Normal	Rheumatic	Hyperpietic	Myocardial	
Supraventricular ..	16	13*	2	3	34
Ventricular	3	0	0	5	8
Number with cardio-grams	19	13	2	8	42
Total number with paroxysms ..	59	19	8	14	100

* Of these 13, 7 were nodal.

CAUSATION OF PAROXYSMS

Although it is important from the practical point of view to decide whether there is organic heart disease or not, this does not explain the initiation of a

paroxysm. There must be some instability of the normal pacemaker, either absolute or relative to other parts of the heart muscle, and this may sometimes be shown by the occurrence of other abnormal rhythms. There was a respiratory sinus arrhythmia of sufficient magnitude to be unusual in 7; and extrasystoles were observed in 26, indicating that parts of the heart other than the S-A node were over-ready to initiate impulses. Two others showed nodal rhythm and sino-auricular block.

Peculiar changes were seen in the cardiogram of one patient. When lying on her right side there was a short P-R interval of 0.08 sec., a large wide R, and an S-T interval below the iso-electric level (Fig. 12). On her left side

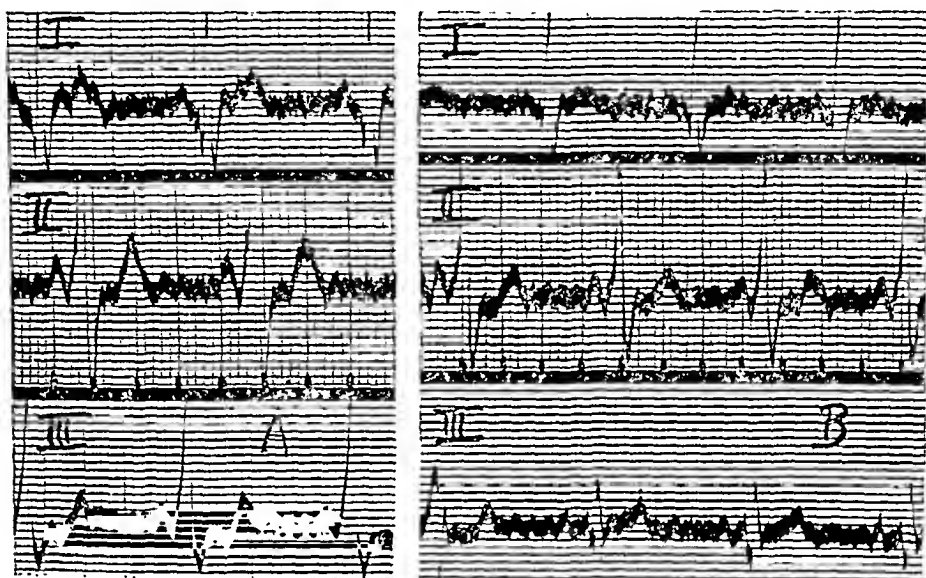


FIG. 12.—Changes which could generally be induced in one patient: (A) lying on the right side; (B) lying on the left side (Case 30).

lead III changed, the P-R interval 0.14 sec., a smaller R, and larger S with upright T waves; the QRS waves varied with respiration more in this position than on her right side. These two types were obtained frequently, and sometimes occurred apart from changes of position, suddenly from beat to beat (Fig. 13). On one occasion the type with a large wide R was obtained by holding her

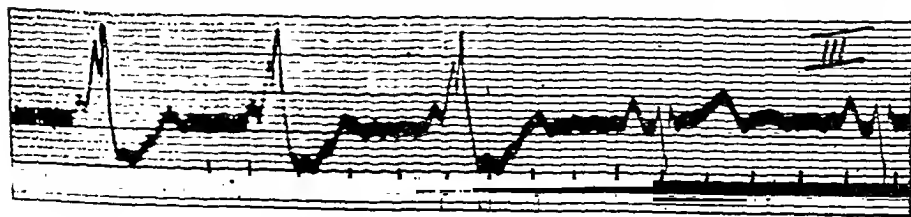


FIG. 13.—Spontaneous changes, illustrating the short P-R interval with complexes of bundle branch block type (Case 30).

breath after a deep inspiration, the S type being present at the beginning and again after expiration.

Wolff, Parkinson, and White (1930) published 11 cases prone to paroxysms with somewhat similar changes, for in the free intervals there was a short P-R interval and a bundle branch lesion, both being abolished by exercise. Evidently the S-A node is in some cases unduly over susceptible to outside influences, such as respiration or changes of position; and in others the relative excitability of the S-A node and the extranodal tissues is altered, extrasystoles resulting.

In addition to this underlying instability, some exciting factor must initiate the paroxysms from an ectopic focus. Many attacks, as is well known, start for no apparent reason and without any warning, but sometimes the patient knows the usual exciting factor, and more rarely may be able to initiate an attack voluntarily.

The beginning or end of a paroxysm are not often recorded except in those studied intensively in hospital, but we were fortunate in recording them in six patients. An unusual type where the onset and offset of short attacks were constantly obtained in many records is shown in Fig. 6; at one time it was hard to obtain a record without these changes, but now seven years later they are less frequent. The end of two attacks and another beginning soon after are shown in Fig. 14; deep inspiration seemed to cause the short returns of

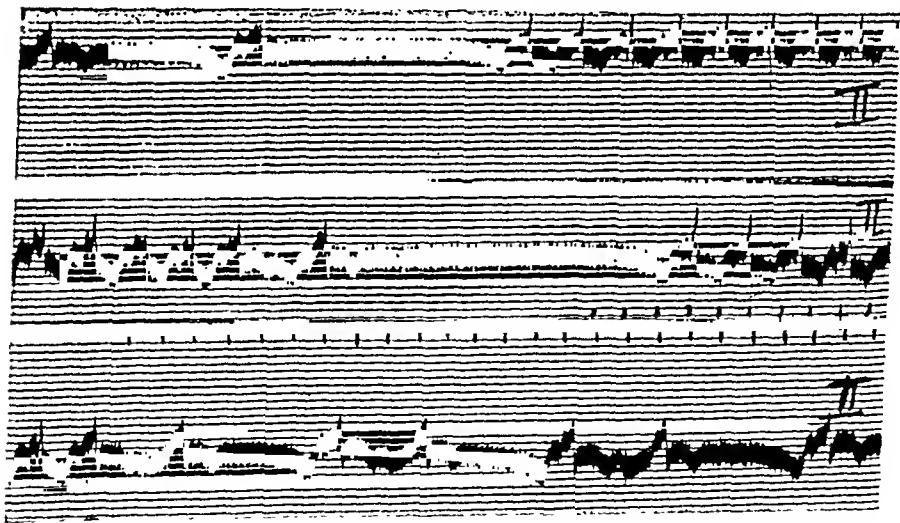


FIG. 14.—Onset and offset of paroxysms, rates 180 and 190, induced by deep breathing; lead II only (Case 82).

normal rhythm. Generally her attacks lasted for many hours, but that morning her condition was specially unstable. Short paroxysms from two other patients are shown in Fig. 15; the first, probably nodal, occurred spontaneously; the second could be produced almost regularly by deep inspiration. Another patient had her first attack when her doctor, examining her lungs after pneumonia, asked her to take a deep breath. The beginning of a paroxysm and a

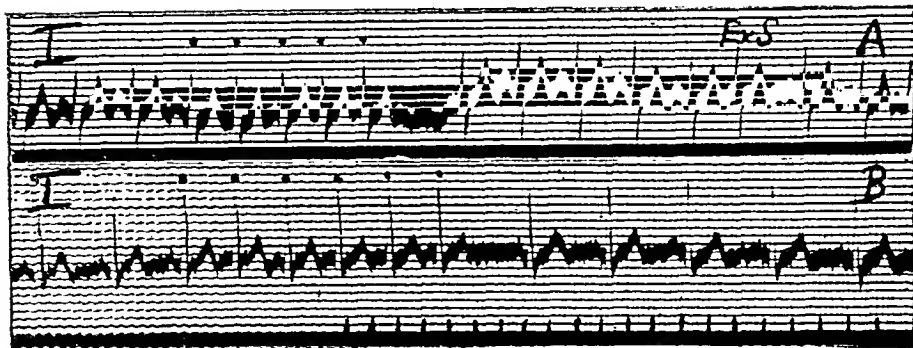


FIG. 15.—(A) Short nodal paroxysm, rate 174, occurring spontaneously in a woman with mitral stenosis (Case 46); (B) Short paroxysm, rate 158, induced by deep inspiration in a woman whose heart was normal (Lead I only).

complete short one are shown in Fig. 16; here again the short attack was exceptional, and there was no obvious exciting cause.



FIG. 16.—Onset of paroxysm, rate 171, in lead I, and complete short paroxysm in lead III; occurring spontaneously in a woman with rheumatic heart disease (Case 60).

A paroxysm interrupting auricular fibrillation is shown in Fig. 17. This was the only time we were able to induce an attack by means of the stimulus

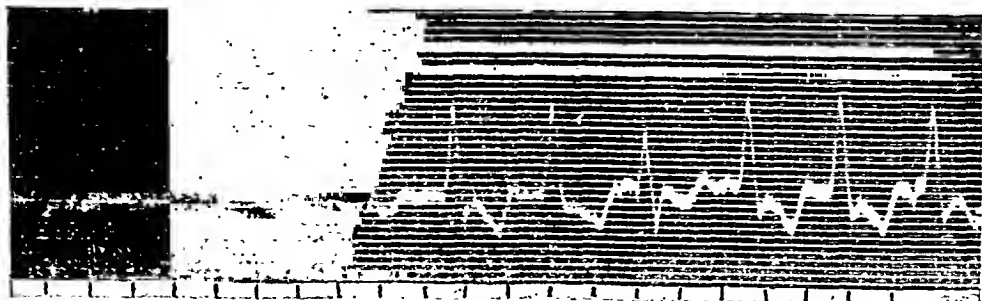


FIG. 17.—Paroxysm at a rate of 141, induced by a loud noise; in a man with established auricular fibrillation and myocardial disease (Case 56). In a long paper tracing the third beat of the paroxysm (shown above the word 'noise') was the only one that differed from the others.

which the patient thought was generally responsible for his attacks—in this instance the unexpected noise of dropping tins on a concrete floor. Another patient attributed several attacks to sudden unexpected noises, such as banging a door.

Sudden movements, such as stooping, turning on one side, jumping, or running upstairs, often start an attack, and where there is an ascertainable cause it is most often of this type. Such movements nearly always provided the stimulus in nine of our cases, for the most part with normal hearts; but similar movements stopped attacks in six others, and this may be useful in advising treatment. One patient was particularly liable to an attack when playing tennis, especially at the moment he raised his arm to serve; he was able to play if he took quinidine before a game. Another had his first attack when he leant out of bed to reach a urinal, and his most recent when he dropped his newspaper in the train and reached down to pick it up.

Such stories are far too common to be due to chance, though often no cause can be detected. Apart from these movements there is a somewhat heterogeneous group of conditions which seem to increase the instability of the S-A node so that any minor cause may excite an attack. Such conditions are anxiety, overwork, over-exertion, pregnancy, obesity, indigestion, smoking, and infection, and these will be considered shortly.

Anxiety.—The patient's state of mind is important. Emotional upsets, excitement, worry due to financial or domestic causes, or anxiety about the supposed gravity of the cardiac state may induce more frequent attacks; in one the first and only attack occurred whilst he was engrossed in a game of chess, and this often happened in another patient. In a bank clerk the heavy work during the period of the War Loan conversion changed infrequent paroxysms into daily events. In many patients the attacks became less frequent and less important when they knew that the heart was otherwise normal. We are speaking of the effect of anxiety on normal people; there is no special association with pathological anxiety states.

Infection.—There is little evidence that infection, acute or chronic, plays any important part. In two patients the first attacks started during convalescence from pneumonia and continued for many years. This might suggest a focus of myocardial damage, but there were no other signs of heart disease, and no such history of infections could be obtained in others. First attacks followed influenza, acute frontal sinusitis, rheumatic fever, tonsillectomy, etc., but six such cases in a hundred is not very convincing.

Chronic focal infections can be accepted as the cause of paroxysms only if their effective treatment produces an improvement. In this series results have been disappointing and no case has shown much improvement. At present there seems no real evidence for an infective group of cases. On general principles focal sepsis should be treated when it is present, but one should never assume that this will cure paroxysmal tachycardia.

Smoking.—There was some improvement in three cases when cigarettes were reduced. Reduction of smoking even down to complete abstinence failed to influence the frequency or severity of attacks in others. There are

people who are unable to smoke because of the frequent extrasystoles induced, and paroxysms of tachycardia occur in some of them ; but tobacco is not often the cause of paroxysms though over-indulgence may increase their frequency.

Exercise.—In six patients attacks were increased by exertion greater than that to which they were accustomed, e.g. working overtime, cross country running, and football when out of training ; and reduction of exercise led to improvement. In two others the first attacks had followed on exercise, in one a game of hockey and in the other long distance running, but they continued without such causes. In two exertion had the opposite effect ; one of them could generally stop an attack by walking or running ; the other, who was leading a sedentary life, was improved by daily exercise. Most of these had no heart disease, but especially in those with rheumatic hearts more frequent paroxysms were often due to their doing more than was advisable for the condition of their hearts.

Indigestion.—No organic disease of the stomach or intestine was found in any of these patients. In two, attacks usually occurred at a fixed time after a meal, and in three a period of indigestion led to an increase in attacks. In two others their frequency was greatly diminished by treatment of their indigestion, but two doctors were disappointed that effective treatment of their indigestion failed to reduce the attacks. Sometimes the disturbance of digestive function produced by the paroxysm is mistaken for its cause. One patient attributed his unusually long attack to indigestion, though he did not usually suffer in this way with shorter ones ; there was, however, congestion of the liver owing to a seven-day attack at a rapid rate. There were severe gastric symptoms, nausea, retching, and vomiting, in eight others. Spontaneous vomiting heralded the termination in three, and induced vomiting was the best method of ending an attack in others. Such symptoms were only observed in a minority, and flatulent dyspepsia is only rarely the cause. Nevertheless enquiries should always be made along these lines, and may reveal an effective method of treatment.

Allergic Conditions.—We have found no association between paroxysmal tachycardia and asthma, urticaria, migraine, or any conditions which are thought to be associated with allergy.

Pregnancy.—Five of these patients and several we have seen since were unfavourably influenced by pregnancy. In three the attacks were more frequent, in two they started at that time. On the other hand, two improved, one for the time and the other after as well as during her pregnancy. Anderson (1932) also has reported a case where paroxysms stopped during pregnancy and (1933) another where they occurred only at this time. In no case in our series except the one described (see p. 156) was there any reason to suppose that pregnancy should have been terminated on account of paroxysms. Meyer, Lackner, and Schochet (1930) reporting two cases stated they had only been able to find four or five examples of paroxysmal tachycardia in pregnancy ; we think they are by no means uncommon and are often mistaken for simple palpitation.

Obesity.—This is mentioned because in two cases, both comparatively young but over-stout, reduction in weight was followed by improvement.

Intrathoracic Disease.—This may cause paroxysms, and two patients, seen since this series, had their first attacks as an early symptom of a mediastinal neoplasm. In two others they occurred during the course of pulmonary tuberculosis. Graber (1925-26) has reported a case where lymphadenomatous glands were pressing on the vagus and we have recently seen an attack in a young man with a Riedel's goitre where the subsequent attacks of pain showed that there was pressure on the vagus. Paroxysmal auricular fibrillation is a more common sequel of thoracic neoplasms, especially when there is a pleural effusion.

SYMPTOMATOLOGY OF PAROXYSMS

Besides the sensation of palpitation complaint may be made of a variety of symptoms, any of which may be more or less prominent and exceptionally may mask the true nature of the paroxysm, especially in children. Rarely the patient may be unaware he is experiencing an attack, when, of course, the diagnosis depends on chance observation. The general symptoms, palpitation, weakness, faintness, dizziness, anxiety, or breathlessness, will not be considered in detail as they are of little special significance in themselves. Any degree of incapacity up to complete prostration may be met with, and may be attributed to any of these sensations. On the whole our experience corresponds with that of other observers—that the incapacity depends mainly on the state of the heart muscle; on the length and to a less extent on the rate of the attack, and on the mentality of the patient.

If the heart is healthy the symptoms are generally discomfort rather than real disability. One man thought it was sufficient if he came out of the scrum and took an easier position in the field when an attack started during a game of Rugby football. Another was able to carry on his routine work at the hospital and lecture, though he certainly found it more of an effort. At the other extreme some patients developed congestive failure. Many of those with rheumatic or other heart disease had little more disability than most of the normals, yet with severe heart disease any attack may be very grave. The importance of the duration and of the rate is discussed later. Shortly one can say that if an attack lasts for one or two days the symptoms and disability generally become important, even if the heart is healthy; and that a healthy heart will support short attacks even at such a rapid rate as 200 surprisingly well.

Loss of Consciousness.—Unconsciousness during the attack is very rare. Two patients, both with heart disease, said that occasionally they had lost consciousness just after the onset. As the hundred cases represent several thousands of attacks, the rarity of loss of consciousness is obvious.

Anginal Pain.—In addition to discomfort or tightness in the chest, present in most attacks and of no special significance, twelve patients had more severe pain of an anginal type during attacks, some occasionally, others when the

the attack had lasted a definite number of hours. In ten it was felt beneath the sternum or just to one side and in two under the left breast ; sometimes it spread down the left arm (five times), down both arms (once), or up into the angle of the jaw (twice). Only in two was the pain really severe, and one of these had angina on exertion apart from his paroxysms. In four where nitrites were used the pain was eased. Seven of these twelve had hearts which appeared normal except for their attacks, and two had mitral stenosis only. The presence of pain, even of a severe type simulating angina, does not indicate an unfavourable prognosis ; this must be judged mainly by the condition of the heart during the free periods. Only one of these twelve has died, six years after the onset of the paroxysms and angina.

White and Camp (1931-32) have drawn attention to the occasional occurrence of anginal pain in paroxysmal tachycardia or fibrillation and the need for distinguishing it from angina of effort, but they do not stress how benign it may be under these conditions. The relationship of paroxysmal tachycardia to coronary thrombosis is discussed later (see p. 148).

Congestive Failure.—This was observed during the attack in nine patients. One, who so far as we could judge had no other evidence of heart disease, had experienced several attacks without failure, but was seen on the eighth day of a ten-day attack with commencing failure, when the rate was 196 and the blood pressure had fallen from 140 to 105. Two children with hearts that were otherwise normal developed failure in attacks lasting two or three days, but the rates were unusually fast. The remaining six had diseased hearts—four myocardial, one rheumatic, and one hyperpætic. In seven the failure became apparent on about the third day, in one with rheumatic heart disease within twenty-four hours. Not many attacks lasting three days were observed in normals, as they were less likely to seek medical advice, but the figures quoted indicate that the development of congestive failure is dependent as a rule on heart disease. Its occurrence does not seem so serious as might be expected, especially where the heart is normal or even well compensated in the free intervals.

THE RATE IN PAROXYSMS

The rate of one or more attacks was observed in 70 cases. It is stated by Lewis (1920) to lie between 160 and 200 usually, with a range from 110 to 220. These upper limits are not high enough, and it is not very rare for the rate to be up to 240 or even faster. In our cases the rate was between 160 and 200 in 45 per cent. and between 140 and 240 in 90 per cent.

In three the rate was less than 140, viz. 136, 126, and 124. The last, who had frequent nodal attacks, is illustrated in Fig. 7. At such a slow rate the diagnosis may be difficult, and here it was not made until she was seen in an attack.

In two children the rate was over 250 (272 and 300, see Fig. 1). They were exceptional in many ways and have been described elsewhere (Campbell, 1937) ; the second may have been paroxysmal flutter. In four others (all supra-ventricular), the recorded rates were 248, 230, 240, and 234 (see Figs. 8b

and 18). Two had no evidence of heart disease and had already had attacks for fifteen and seventeen years. The other two had rheumatic lesions.

TABLE V
HEART RATE IN PAROXYSMS

Type of Paroxysmal Tachycardia	Number of cases recorded at each Rate							Total
	120-139	140-159	160-179	180-199	200-219	220-239	Above 240	
Nodal	2	5	5	1	2	2	0	17
Other Supra- ventricular ..	1	6	6	5	3	3	3	27
Ventricular ..	0	1	2	3	3	1	1	11
Paroxysms with- out a cardio- gram	0	3	8	8	6	3	2	30
Total	3	15	21	17	14	9	6	85

Table V summarizes the findings and shows how the rates were distributed among the different types of paroxysms. There were cardiograms of 55 attacks from 42 patients (two from the same patient being counted because the rate was sometimes different), and of 30 others observed clinically. Slow and fast rates were found in each type. Analysis in various ways shows few conclusions except that nodal attacks tend to be a little slower and ventricular attacks a little faster; and that sometimes it is a bad sign when the rate of the attacks in any patient falls during the course of months or years.

In the nodal attacks the average rate was 170 and the commonest range was 140 to 180; one fallacy may be that at the slower rates it is easier to distinguish the P wave and so to diagnose nodal tachycardia. In the other supra-ventricular attacks the average rate was 187 and the usual range was 150-230 with more below 190. In the ventricular the average was 198, the usual range was the same, but more were above 190.

The presence or absence of disease did not appear to influence the rate, the average for the normal cases being 190, for the rheumatic 178, for the myocardial 180, and for the hyperpietic 185. The range in all the larger groups was much the same and included fast and slow attacks.

The rate in different attacks is said to keep about constant. This is our general experience and cardiograms obtained in different attacks from several cases were practically identical after an interval of years. In many patients, however, they varied by as much as 10 to 15 per cent. In short attacks the rate may vary considerably within a few minutes. Here it may represent a different ectopic focus.

Where rates were accurately observed in several paroxysms one third showed a difference of between twelve and thirty beats per minute; most of these had heart disease. The period over which paroxysms have occurred did not in itself cause a change in rate. The changes were not more common

in any one type of attack or in different diseases of the heart. There was some evidence that as the efficiency of a diseased heart lessens, the rate of the paroxysms may fall ; but others observed up to the time of death maintained a constant rate to the end. For example, in two a fall of 12 and 30 beats per minute preceded the onset of fibrillation, and in two others the rate slowed as they became worse—26 and 22 beats per minute. An increase in rate as the myocardium fails is less common.

Comparing the rates recorded graphically with those counted personally, there is no reason to think that the "clinical" rates are not accurate, except that there were fewer under 160, perhaps because paroxysms at a slow rate are less likely to be diagnosed without a graphic record. The rate should always be taken for half a minute. Generally when the rate is said to be uncountable it is because an attempt has been made to count the pulse by the finger instead of the heart by the ear.

THE LENGTH OF ATTACKS

Paroxysms last for hours much more commonly than for days. Though variable, they tend to have a more or less customary length in any one subject, who can generally report that the attacks last between, say, two and eight hours, or less than half an hour, or more than a day, and is surprised if his past experience does not prove a useful guide of what to expect. In two patients, for example, the length of many of their attacks were recorded over a series of years. In one (Case 30) there were 122 paroxysms in eleven years (1927–38) and the length of 89 of these known ; the number of paroxysms of different lengths was as follows :

1-4 hours	8
5-8 "	19
9-12 "	24
13-16 "	14
17-20 "	5
21-24 "	10
25-48 "	7
17 and 29 days	2

In the other (Case 70) the length of 88 paroxysms in the years 1924-32 was recorded as follows :

Less than $\frac{1}{2}$ hour	55
$\frac{1}{2}$ -1 $\frac{1}{2}$ hours	15
2-3 "	9
4-5 "	8
8 "	1

In these two, though there is variation round the customary length in each case, it is easy to give an average range and to say that what would have been a long attack for one would have been a short attack for the other.

More than half of these patients generally had paroxysms of less than two

hours, and in seven only did they habitually last for a day or more, even though those with longer attacks are more likely to come under observation. Table VI shows their usual duration in this series, though often it was difficult to decide such precise limits. The longer attacks occurred a little more often in those with heart disease, but the difference was not great.

TABLE VI
THE CUSTOMARY LENGTH OF PAROXYSMS IN 100 PATIENTS

The Customary Length of Paroxysms	Patients with no Heart Disease except the Paroxysms	Patients with Heart Disease	Total Number of Patients
Up to 30 minutes	23	12	35
" 2 hours	15	11	26
" 6 hours	12	6	18
" 12 hours	5	5	10
" 24 hours	1	3	4
Over 24 hours	3	4	7
Total	59	41	100

The longer paroxysms are of more importance, for the distress and disability and even the likelihood of congestive failure are increased. In addition to the 7 that habitually had attacks lasting more than twenty-four hours, 22 others had some of this length, making a total of 29 with some or all of their attacks lasting more than a day. The attacks were not often this length and never greatly exceeded it in ten of these, six with heart disease and four without, and did not produce serious symptoms, or any change in the general condition.

The remaining 19 with long attacks are illustrated in Table VII. There were six (including two small children) with hearts that were normal except for the paroxysms and four with rheumatic heart disease, most of the remainder falling into the myocardial group. The long attacks were least frequent in those without other evidence of heart disease—11 per cent. of the normal, 21 per cent. of the rheumatic, and 33 per cent. of the other groups having these long attacks.

The rate in these longer attacks was generally faster than the average for all the paroxysms; in only three was it under 180 and in ten of the nineteen it was 200 or over, while among the other cases there were more under 180 than at 200 or over. The average rate in these long attacks was 208 (or 198 if the two exceptionally fast ones be excluded), instead of 186 for the series as a whole. All types of attacks were represented, but there was a much higher proportion of ventricular paroxysms than of the other types, nearly half the former lasting for more than twenty-four hours.

Even among these longer attacks relatively few lasted for more than two or three days, and they were of this length in eight patients. In two they lasted 4 days; in two up to 7 days; and in five, 10 days; only in two did they last longer than 10 days. One of these (Case 15) is described in the

TABLE VII
PAROXYSMS OF UNUSUAL LENGTH

Case Number	Age	Ætiological Group	Paroxysms		Length of Paroxysms	
			Rate	Type *	Usual— in hours	Less Usual
<i>Seven patients whose paroxysms generally lasted more than 24 hours</i>						
5	21	Myocardial	210	V.	Three attacks only of 5 to 10 days.	
15	24	Myocardial	190	—	8-48	7-8 days, three 14 and 17 days and 4 weeks
69	1	Normal	272	V	48	Several days.
78	1	Normal	300	S.	Two attacks only of 3 days.	
84	27	Rheumatic	175	N.	6-48	Up to 7 days.
85	20	Rheumatic	200	S.	12-36	Up to 4 days.
88	40	Normal	—	—	10-30	Up to 3 days.
<i>Twelve patients whose paroxysms generally lasted for a few hours only</i>						
11	30	Myocardial	205	V.	1-6	Several of 10 days.
16	53	Myocardial	160	—	12-24	One of 7 days.
30	17	Normal	220	S.	10-18	Two 29 and 17 days ; several 36-50 hours.
36	44	Rheumatic	240	S.	1-1	One of 2 days.
37	47	Syphilitic	—	—	2	One of 2 days.
43	48	Normal	190	S.	1-6	One of 10 days ; several 1-2 days.
55	41	Myocardial	200	—	4-12	Several of 3 days.
			172			
61	50	Hyperpætic	to 204	—	1-48	Several over 2 days.
68	25	Myocardial	200	—	Variable	Four attacks 7-10 days.
75	20	Normal	180	—	1-3	Sometimes up to 3 days.
80	41	Rheumatic	217	N.	1-1	Sometimes up to 4 days.
82	12	Normal	197	S.	2-12	Some up to 7 and 10 days.

* N, nodal ; S, supraventricular ; V, ventricular paroxysms.

section on prognosis ; an attack in which congestive failure developed lasted 17 days. There had been shorter ones for sixteen years, but longer attacks recurred and he died five years later in one that lasted more than 28 days. The other, aged 38, had suffered from attacks for twenty years and during five years' observation had about ten a year lasting generally for 10-18 hours and never more than 48 hours. She was admitted to another hospital when one attack had lasted 24 days and the heart rate remained over 200 in spite of treatment with digitalis. As it still continued after 29 days she was transferred to Guy's Hospital, but it stopped during her journey. She soon felt as well as usual, though for a few days the T waves were rather flatter. The frequency and duration of her paroxysms were not permanently increased (see Table IX), and in other respects her heart could be passed as normal. After another seven years she had a second long attack of 17 days treated with digitalis in her local hospital. A cardiogram of a subsequent attack showed no evidence of progressive myocardial disease as it was almost identical with the first of 1927 (Fig. 18), except for some left axis deviation.

These attacks of exceptional length are very unusual and naturally more serious, but it is possible for them to occur without there being any disease of

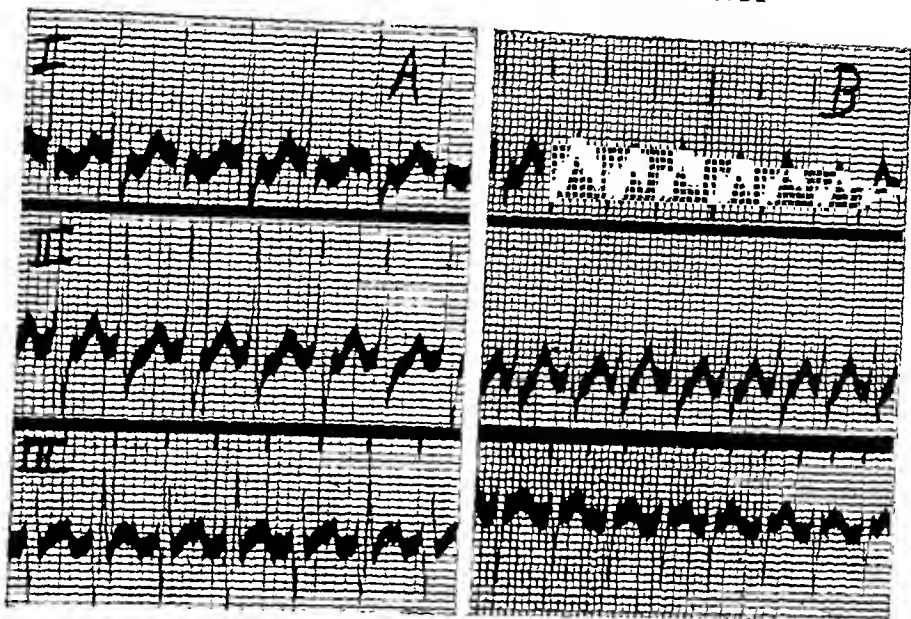


FIG. 18.—Two paroxysms from the same patient : (A) in 1927, rate 230 ; (B) in 1938, rate 207, (Case 30).

the heart and for complete recovery to take place. The great majority of paroxysms last for hours rather than for days, but 30 per cent. of our patients had one or more attacks lasting for a day, 10 per cent. of these very rarely, 10 per cent. occasionally, and 10 per cent. habitually. Only two had attacks lasting longer than ten days, though Gallavardin (1930) in a paper on paroxysmal tachycardia of long duration found that 11 out of 160 cases had some attacks as long as this.

TREATMENT

The treatment of the patient during a paroxysm and his management during the free intervals must be distinguished.

During an attack rest should generally be advised, but rest in bed is not needed unless special symptoms or the condition of the heart at other times make it advisable. Pressure on the vagus or on the carotid sinus is often effective, and also many tricks of sudden movement (e.g. bending down to open a low drawer) ; perhaps a forced expiration with a closed glottis after a deep inspiration is the most generally successful. If an attack persists towards evening, bed with a sedative or hypnotic will generally lead to its arrest.

Quinidine, 5 grains, repeated if necessary in two hours, is probably the most useful medicinal treatment. The cessation of attacks after digitalis has often been reported, but it is doubtful if it is effective, and generally it should not be given unless indicated by the state of the heart apart from the paroxysms or by the development of failure in a long attack. If there is any likelihood that the attack may be paroxysmal auricular flutter, full digitalization is indicated, both from the point of view of diagnosis and treatment.

Of newer remedies mecholin, 15 mg. intramuscularly, has often been successful in reported cases, but has been unpleasant and not very successful in our experience. So far prostigmin, 0.5 to 1.0 mg. subcutaneously, has seemed to us more effective and harmless to use ; but it is early to decide its special indications and limitations. Morphia is not desirable in ordinary recurrent attacks, but may be used and may be effective if an attack is causing serious anxiety to the medical attendant.

After the paroxysm the most important question is to decide the condition of the heart. If thorough examination justifies it, reassurance about the nature of the attacks is often all that is called for, and this alone will sometimes greatly diminish their incidence. The general regulation of the patients' life as regards food, work, and exercise must next be attended to, and in many cases a sedative such as bromides will be all else that is needed. If in spite of this the attacks are frequent and troublesome regular administration of quinidine for a time, 3 to 5 grains, t.i.d., will often succeed. Regular digitalization is rarely indicated and has not been useful in our experience. Several cases where these methods have been successful and some where they have not are given in this paper, especially in the section on course and prognosis.

COURSE AND PROGNOSIS

The Immediate Outlook at the time of a Paroxysm.

This is excellent, and however long a paroxysm has lasted, whatever the rate, and however ill the patient may seem, he may be expected to recover. The only exceptions are if the paroxysms are of the rarer ventricular type, or occur after the heart has begun to fail, or in the course of coronary thrombosis ; even so, though the risk is greater, he will generally recover from the immediate attack.

It is often stated that a patient may die in a paroxysm ; this is rare, and it creates just the impression it is necessary to avoid in the large majority, where there is no danger. Only five in this series of a hundred have died suddenly or during a paroxysm, including one from an overdose of morphia and one after a miscarriage ; and four of them had been liable to paroxysms for long periods (two for over 20 years and two for nearly 10 years) and had had hundreds of attacks before their deaths. Only one died soon after the onset of his paroxysms. Two at least, including the last, had ventricular paroxysmal tachycardia, and almost certainly died with ventricular fibrillation (Cases 5 and 79). A boy of seventeen under the care of Dr. Parkinson, who had suffered for five years from long and frequent ventricular paroxysms with gross congestive failure, provides more definite evidence. After an ordinary day with a short attack in the morning, he suddenly said that his heart had stopped and fell down dead, apparently after only a few breaths. From his words he must have known this was something quite different from the usual attacks and it was probably ventricular fibrillation. Because of this possibility the outlook in ventricular paroxysms is more serious, and this is one reason for trying to obtain an electrocardiogram of the paroxysm ; fortunately they are

much less common. With supraventricular paroxysms the outlook is excellent, apart from other unfavourable findings in the heart.

It is equally important when the attacks are only of recent onset to decide if they may indicate progressive heart disease. The age of the patient is some help, and of those whose first attack came after 40, only 25 per cent. had normal hearts; while of those under 40, more than 60 per cent. had normal hearts. The following is an instance where paroxysms were the first symptom of commencing disease of the coronary artery. A man of 54 had a few paroxysms lasting two hours; he had no pain and no cardiac symptoms previously. After a year he began to get angina of effort, and during the next two years this was induced more easily by diminishing amounts of exertion. There have been no further paroxysms. This is an important and not uncommon variety; if paroxysms are of recent onset they are much more likely to be associated with organic heart disease in the elderly than in the young.

When a paroxysm occurs after coronary occlusion the immediate prognosis is not as bad as might appear, though it must add to the gravity. It generally stops spontaneously or after treatment, and the outlook depends more on the extent of the infarct. By chance none of these cases were examples of paroxysmal tachycardia secondary to coronary thrombosis, but one seen since illustrates the association. A man of 52 had a severe cardiac infarct, with pain for several hours in spite of morphia. His progress was satisfactory for ten days, until ventricular paroxysmal tachycardia started at a rate of 148. Quinidine, 30 grains daily, failed to arrest it, and he died after it had persisted for sixteen days. If, therefore, the patient is seen for the first time during a paroxysm, it is wiser not to make a final diagnosis of the heart condition at once. Murmurs may be difficult to hear, and if it has lasted long the blood pressure may have fallen and the heart may be dilated. The cardiogram may be abnormal for a few days after a long attack, so the complete examination should take place later than this. If at this stage the condition of the heart does not warrant a bad prognosis, the paroxysms may be looked on as an inconvenience rather than a serious matter.

The Ultimate Prognosis

This depends mainly on the condition of the heart in the free intervals, and to a lesser extent on the future frequency of the attacks and the effect, if any, they may have on the heart. Over 80 per cent. of these patients have already had attacks for more than five years and 47 per cent. for more than ten years, so that there has been ample opportunity to observe any unfavourable changes. The period which has elapsed since the onset of their paroxysms is shown in Table VIII. In the second and third columns they are divided into those who were alive when last heard of and those who have died, most of the deaths being due to the general course of their heart disease. In the last three columns they have been divided into three groups, those with no heart disease (including four with goitre), those with rheumatic heart disease, and those with hyperpietic

or myocardial disease ; as would be expected, the results are very different in these three groups.

TABLE VIII
LENGTH OF LIFE AFTER THE ONSET OF PAROXYSMS

Number of Years since onset of Paroxysms	Number of Cases			Number of Cases		
	Still living	Dead	Total	Normal group	Rheumatic group	Myocardial and Hyper-pietic group
Up to 5 ..	16	2	18	13 —	3 —	2 (2)
5-9 ..	28	7	35	18 —	6 (2)	11 (5)
10-14 ..	13	3	16	10 —	2 (1)	4 (2)
15-19 ..	10	0	10	4 —	4 —	2 —
20-24 ..	4	1	5	1 —	2 —	2 (1)
25-29 ..	9	2	11	8 (2) *	2 —	1 —
30-39 ..	2	0	2	2 —	— —	— —
40-49 ..	0	0	0	0 —	— —	— —
50 and more	2	1	3	3 (1)	— —	— —
Total ..	84	16	100	59 (3)	19 (3)	22 (10)

* The numbers in brackets indicate those who have died.

1. *Normal Group.*—Where the heart was otherwise normal, serious complications were rare and a decrease in the frequency of the attacks from some change in the patient's life was quite as likely as an increase. The follow-up of these patients and close contact with many of them for years has convinced us that as a rule paroxysms do not cause progressive deterioration and still less disease of the heart, though some are very resistant to treatment and continue to have paroxysms with the same frequency over many years. Some examples may be given.

In one patient paroxysms started when he was 9 and continued through life. A few months before his death at 69, although he had developed lymphatic leukæmia which was held in check by deep X-ray therapy, he had no signs of heart disease, a normal electrocardiogram with good T waves, and was able to lead an active life (Case I).

Another started having paroxysms when 50 ; at 75, though they were rather frequent and he had suffered from an enlarged prostate for seven years, he was still in business and did not notice any dyspnœa. There were no signs of cardiac or arterial disease, and his cardiogram was normal except for ventricular extrasystoles. He died three years later a few days after prostatotomy (Case 51).

A third was 68 when he was first seen and paroxysms had started at 23 ; they lasted up to two hours and he was rarely two weeks without. He was treated with bromides and luminal, and at 75, though his blood pressure was 180/110 and his heart a little enlarged, he had no complaint except of "a dulcimer constantly playing all the old tunes that had run through his life" ;

this had started two years before and was associated with increasing nerve deafness. His paroxysms were shorter and less severe (Case 66).

The cardiograms of these three cases are shown in Fig. 19.

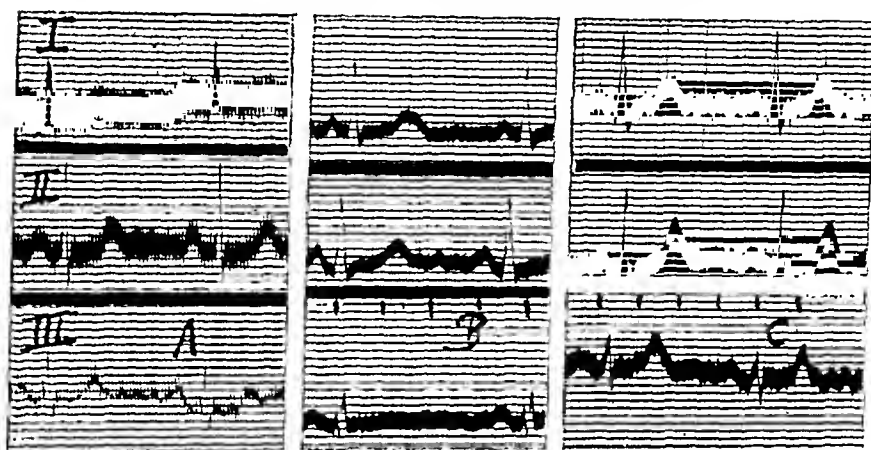


FIG. 19.—Normal electrocardiograms from three men who have had paroxysms for (A) 60 years (Case 1, aged 69) ; (B) 55 years (Case 66, aged 74) ; and (C) 28 years (Case 51, aged 75).

A fourth started having attacks when he was 7, and has rarely been three months without and sometimes has two or three in a month, lasting three to four hours or less commonly a day. He was seen when 56 with slight dyspnoea, with his aorta a little dilated and with broad QRS complexes in the cardiogram—findings which are not rare at his age. After another 10 years he has not aged much and there has been no substantial change in the condition of his heart or of his paroxysms, and he still leads an active life. He may die of heart disease, but in view of his long story this appears incidental (Case 89).

Table IX shows the frequency and length of paroxysms in a patient on

TABLE IX
FREQUENCY AND LENGTH OF PAROXYSMS IN CASE 30

Year	Number of Attacks	Length of Attack in Hours		
		Average	Usual Range	Total Hours
1927	6	13	10-16	81
1928	7	14	10-18	97
1929	10	17	13-24	173
1930	7	16	14-18	112
1931	16	20	12-24	320*
1932	7	21	8-48	146
1933	10	17	8-48	166
1934	19	9	4-12	164
1935	12	13	4-48	156
1936	11	9	6-12	103
1937	5	20	8-24	98
1938	4	25	12-36	76†

* Excluding attack of 29 days.

† Excluding attack of 17 days.

whom no treatment, medicinal or general, has had any influence. But after 29 years of paroxysms her health has not been impaired and during 12 years' observation there has been no progressive increase in their frequency.

All these were free from organic heart disease. Three others are still without any signs of heart disease or of impaired health after more than 20 years of attacks.

2. *Rheumatic Group*.—Here paroxysmal tachycardia might be expected to be more serious, but generally this was not so. Most of the rheumatic patients have been satisfactory (see Table VIII), and they have done as well as could have been expected had they been free from paroxysms. Details of three follow: the first was one of the few instances where her progress was downhill from about the time the paroxysms started; the second was successfully treated with quinidine; the third was not influenced by treatment, but got on well for eleven years with paroxysms and for another nine with fibrillation.

A woman of 35 with mitral stenosis had her first paroxysm while hop-picking, and subsequently short attacks occurred frequently up to three or four daily. Three years later fibrillation became established and she responded well to treatment with digitalis, but after another two years abandoned treatment for months and was admitted with congestive failure and a cerebral embolism, and died after three weeks. Autopsy showed extreme mitral stenosis, left intra-auricular thrombosis, and pulmonary infarcts (Case 46).

The second had rheumatic fever at 21 and paroxysms started at 33, after her third pregnancy. At 46, when first seen, the heart was slightly enlarged, with aortic incompetence. For 8 years most of her attacks were reported and their frequency and duration, shown in Table X, were greatly reduced with quinidine; when this was stopped they became more frequent, after which she again resumed quinidine with success. Several attacks were observed, always at about the same rate, those recorded

TABLE X
FREQUENCY AND LENGTH OF PAROXYSMS IN CASE 70, SHOWING THE INFLUENCE OF QUINIDINE

Date	Period of Time in Months	Number of Paroxysms	Average per Month	Average Length in Hours (approx.)	Treatment
1924-25	10	39	3.9	1.5	—
1925-26	15	20	1.3	1.0	Quinidine, grs. 5.
1926	2	10	5.0	0.5	Pol. brom., grs. 45.
1927	4	6	1.5	0.5	Quinidine, grs. 5.
1927	2	20	10.0	0.5	Gentian and soda.
1927	7	16	2.3	1.5	Quinidine, grs. 5.
1928	12	13*	1.1	0.5	Quinidine, grs. 10.
1929	12	4†	0.3	2.0	"
1930	12	6	0.5	3.0	"
1931	12	4	0.3	1.5	"
1932	12	3	0.2	1.5	"
1933-35	36	15	0.4	—	"
	122	85	0.7	1.5	With Quinidine.
	14	69	5.0	1.0	Without Quinidine.

* Including 6 in two weeks with influenza.

† Excluding several short attacks in two weeks with influenza.

clinically at about 240, those recorded graphically at 232, 225, and 233 (Fig. 8b). Her condition 14 years after she was first seen had not changed for the worse, and with ten grains of quinidine daily her attacks were still well controlled, about one each three months. Her blood pressure was almost the same as 14 years before and the heart seemed little larger. A paroxysm was recorded at a rate of 210, rather slower than before (Case 70).

The third had rheumatic fever when 5 years old, after which she was slightly short of breath. At 20 she had sudden palpitation when walking upstairs, and following this attacks lasting from one to twenty-four hours. She was first seen when 29 with a rather large heart and with mitral and aortic lesions. Paroxysms occurred frequently (Fig. 8a) and were not reduced in frequency by strophanthin, digitalis, or quinidine; perhaps they were least frequent when she was taking bromides. Generally she had one or two attacks a week, and there was little change for two years. Fibrillation then became established when she was 31; the paroxysm before this lasting four days and seeming different because her heart had been irregular (paroxysmal fibrillation). Nine years later, after marriage and three years in India, fibrillation was still well controlled with digitalis (Case 52).

Paroxysmal Tachycardia and Auricular Fibrillation.—The relationship between these two may be considered here as it concerns rheumatic patients mainly. There is some connection, though it is not very close. Paroxysms interrupted fibrillation in one patient (Fig. 17). There were 7 others, 5 with rheumatic heart disease and 2 without, where fibrillation eventually became established and details are shown in Table XI. Another after having paroxysms

TABLE XI
ESTABLISHED AURICULAR FIBRILLATION FOLLOWING PAROXYSMAL TACHYCARDIA

Case Number	Heart Disease	Sex and Age at Onset of Paroxysms	Duration of Paroxysms before Auricular Fibrillation (in years)	Duration of Auricular Fibrillation (in years)	
				Patients who are dead	Patients who are alive
24	Mitral stenosis	F. 27	13	—	5
46	Mitral stenosis	F. 35	3	2	—
52	Mitral stenosis	F. 20	10	—	10
77	Aortic stenosis and incompetence	M. 40	28	—	1
80	Mitral stenosis	M. 42	8	—	1
38	Myocardial	M. 64	2	4	—
98	Normal	M. 57	6	—	3*

* Onset of fibrillation after an operation for pyonephrosis; quinidine restored normal rhythm for a time only.

for twenty-four years began to have these interspaced with paroxysmal auricular fibrillation (both recorded); she still maintains normal rhythm after another three years (Case 70, Table X). A woman of 42 who had rheumatic fever when 21 sometimes changes at the end of her paroxysms to fibrillation. In one attack she was given quinidine and one and a half hours later her heart was irregular (Fig. 20); she said it was often like this towards the end (so it was not entirely due to the quinidine) and that if she kept still it would prob-

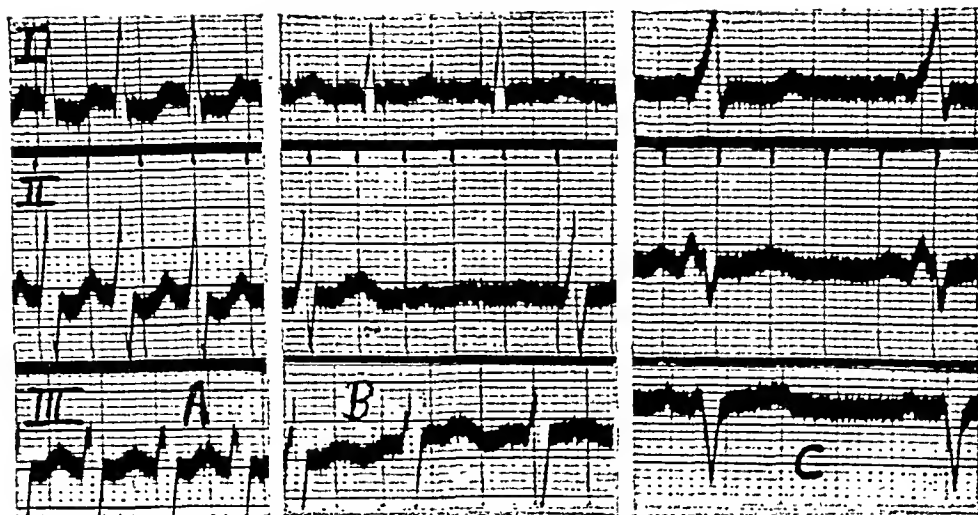


FIG. 20.—(A) Paroxysmal tachycardia, rate 214, from an obese woman with a rheumatic history; changing into (B) paroxysmal auricular fibrillation, rate about 103; and ten minutes later to (C) normal rhythm, rate 75.

ably stop. With great care she was moved to the galvanometer, which confirmed fibrillation, and in ten minutes normal rhythm returned (Fig. 20). Paroxysms of fibrillation in a rheumatic case often indicate that this rhythm will be established in the near future (Parkinson and Campbell, 1930); but this is not true of paroxysmal tachycardia.

3. Hyperpietic and Myocardial Groups. These patients have done less well than those with normal or rheumatic hearts, as nearly half of them have died. Two had syphilitic heart disease and eight had high blood pressure; in none of these did the occurrence of paroxysms seem of special significance, as the four who have died had serious heart disease which appeared to run its usual course. The other six in spite of their paroxysms have continued in moderate health—one after 26 years and another after 15 years, but possibly these two ought to be transferred to the normal group as the blood pressure may have developed later than and independently of the paroxysms. In all the prognosis was that to be expected from the condition of the heart quite apart from the paroxysms.

The myocardial group must be considered in rather more detail, and in view of the more serious outlook it is noteworthy that four of the eight with ventricular paroxysmal tachycardia belonged to this group. Four of the twelve in the myocardial group were elderly patients and would probably have come under observation for their heart condition quite apart from the paroxysms, which were unimportant compared with the other symptoms and findings; three of these have died.

The fifth was 58 and would not have been seen but for his paroxysms. Although he had no other symptoms his heart was enlarged and the cardiogram showed biphasic T waves in lead I and widened QRS complexes. Even so, although one paroxysm lasted nine days and led to congestive failure, they have not proved serious, since after six

years he is still well, with no progressive changes in the cardiogram or in the size of the heart (Case 16).

Three others would have passed as normal except for the cardiograms in the free intervals ; as all were between 26 and 40 the abnormality is the more remarkable. The changes that may be found in the cardiogram for hours or days after a long attack were not regarded as proof of heart disease, though they mean that this possibility has to be excluded with care.

One had a tuberculous hip excised when he was 11 and at 30 had his first paroxysm. Generally they lasted for an hour only, but on five occasions for seven to ten days so that he was in hospital. The abnormal cardiogram was the only evidence of heart disease, but now after 15 years he is becoming short of breath on exertion. He has some calcified areas in the mediastinum and at the apices of the lungs, so possibly some tuberculous disease spreading to the pericardium may be responsible for his paroxysms and for the abnormal cardiogram (Case 11).

One started having paroxysms when she was 12 years old. She was seen when 27 because although they were not frequent and only lasted five or six hours she felt ill for some days after them. Nothing was found except scoliosis and a cardiogram with flat T waves and rather wide QRS complexes. Five years later she was better, her attacks shorter, and her cardiogram more normal (Case 6).

The third has more frequent attacks which have ceased to trouble him since he found that they can be stopped easily by bending down to open a low drawer ; he has no other symptoms, but his cardiogram is still not normal (Case 68).

In the last two the abnormal signs in the cardiograms have become less, and now after six years they are in good health and without other symptoms. Possibly the paroxysms and abnormal cardiograms were the only signs of a temporary myocarditis from which there has been good recovery. Another patient, included as normal because nothing can now be detected in his heart (Case 43), had his first paroxysm when he leant out of bed during his convalescence from pneumonia ; he may have had a pneumococcal myocarditis and recovered completely except for the tendency to paroxysms, but there is no proof of this.

The remaining four (Cases 5, 15, 79, and 81) had abnormal cardiograms and some enlargement of the heart without obvious cause. Their ages when first seen were 21, 39, 37, and 18. They form an important sub-division as they include three of the five patients who have died suddenly or during attacks. All are fully described in the next section and in two the fatal result was probably due to ventricular fibrillation associated with ventricular paroxysms. The third is more disturbing because he provides the only instance where death was due to a paroxysm without the certainty of preceding heart disease, and where such changes as were found seem to have been caused by the paroxysms rather than to have caused them—a process which might be expected on *a priori* grounds, but is in our view most exceptional. Paroxysms had occurred for 21 years, and where so little could be found at the autopsy it is unlikely the enlargement of the heart was present at the start or that there could then have been any coronary disease ; the simplest explanation seems to be that attacks which were inconvenient rather than serious for 15 years began to last longer and to produce congestive failure, and that one lasted long

enough to cause his death. Without this case, we should have said more dogmatically that paroxysmal tachycardia alone never proved fatal. Even with myocardial disease, slight or serious, the prognosis is generally that of the heart disease and is not much affected by the paroxysms.

Patients who have Died

Some details about the 16 deaths during the period of observation (1925-38) will be given. At first sight this number suggests a bad prognosis, but in 4 the cause of death was nothing to do with the heart and in 7 others their length of life was quite up to the natural expectation of their heart disease, had there been no paroxysms. In 5 of the 16, however, death took place during a paroxysm and these must be considered fully, as even 5 out of 100 would be a serious proportion, were there no other reason for the deaths.

Two of the 4 patients whose deaths were not due to their hearts had suffered from paroxysms for 60 and 28 years and died from leukæmia and after prostatectomy respectively ; neither had any signs of heart disease even near the end of life. (Cases 1 and 51, see p. 149.) The third died two years after an operation for cancer of the breast with recurrences ; paroxysms are not uncommon when there are secondary deposits in the thorax, but here they occurred for some years before the neoplasm. The fourth died two years later from cerebral hæmorrhage.

In 7 patients death was caused by heart disease, but its course did not seem to be influenced by the paroxysms. One had a blood pressure of 200/110 and pulsus alternans ; a second, whose paroxysms began after fibrillation had been arrested by quinidine, died six years later with congestive failure ; a third had severe angina for six years before his death from coronary occlusion ; and a fourth had syphilitic aortic incompetence and an aneurysm. Two had rheumatic heart disease : one, with mitral stenosis and paroxysms for three years, died two years after the onset of fibrillation ; and the other, with a large heart and mitral and aortic lesions, lived eleven years after the onset of frequent paroxysms ; the seventh (Forman, 1931) had a calcified pericardium and died five years after the onset of his attacks.

So far as we know none of these 11 died unexpectedly or during paroxysms and we have no reason to think the length of life was shortened by them, though sometimes they were the first sign that the condition of the heart was starting to go downhill. This may be so, but is by no means the rule, and many patients with heart disease have done well without any progressive loss of reserve.

The remaining 5 are more significant, since they died suddenly or during paroxysms. The only one of these five that was thought to have a normal heart almost certainly died from an overdose of morphia. Of the other four two died suddenly and two with congestive failure.

The first was seen when his attacks, though infrequent, had already been present for 15 years ; and after another 11 years his wife wrote to report his death in a paroxysm. To further enquiries his doctor replied that as on previous occasions when

called in he had given half a grain of morphia, saying it was sufficient for the night ; but the patient had sent for a second doctor, who, unaware of the previous treatment, had given another injection of morphia, which probably caused his death (Case 28).

The second had mitral stenosis and moderate enlargement of the heart, and her supraventricular paroxysms began when she was 27 ; at 36 they had not greatly changed her condition and recurred about each six weeks and lasted for six to forty-eight hours (once seven days). She was admitted to hospital on the fourth day of an attack in the fourth month of pregnancy with anæmia and commencing failure, and as all efforts to stop it were unsuccessful her failure became worse. She lost a good deal of blood after a miscarriage and died on the seventeenth day. Here the attack was the immediate cause of the failure which led to her death, but the anæmia and the miscarriage were complicating factors (Case 84).

The third died suddenly when he was 45. He was refused for the army at 18 because of his heart, and again during the War at 26 ; he had some dyspnœa and palpitation, and when 37 lost consciousness after a paroxysm. Seen two years later, after a similar attack, he had a large heart mainly to the left, a loud systolic murmur, some widening of the aorta without high blood pressure, and a partial bundle branch block, and it was difficult to decide the exact nature of his heart disease. Several short paroxysms of ventricular tachycardia were observed at a rate of 186. Six years later we learnt that he had died suddenly while carrying an electric cooker downstairs. The coroner kindly supplied this report—"Heart 540 grams, hypertrophy and dilatation, chiefly of ventricles ; muscle thin and flabby with fibroid degeneration ; mitral and tricuspid valves themselves normal but incompetent ; coronary arteries moderate atheroma, orifices narrowed ; no rheumatic or syphilitic disease." Here it seemed probable that disease of the coronary arteries started at an early age and progressed till it led to his death. He was never an example of the common type, where the paroxysms were the main presenting symptom, because the physical signs and dyspnœa which led to his rejection from the army were present several years before the paroxysms (Case 79).

The fourth also died suddenly. His health had always been good except for diphtheria at 9, when he was in bed five months with paralysis of the soft palate and dilatation of his heart. Though some extrasystoles persisted he became free from symptoms, and when 19 took up heavy work, lifting crates that weighed 72 lb. ; he was able to carry on with this and with boxing and football without dyspnœa. When he was 21 he woke up in a paroxysm, which lasted ten days at a rate of about 200. After three weeks he felt fit and returned to work, but had shorter attacks of one and five days. When first seen five months later, his heart rate was 72 with frequent extrasystoles. The blood pressure was 120/85, and there were no physical signs except slight enlargement of the heart. His cardiogram showed poor T waves and ventricular extrasystoles of two types. He was admitted to hospital next day, with a ventricular paroxysm at a rate of 220 (Fig. 3) ; the blood pressure was under 100, and already there was some enlargement of the liver and slight œdema of the feet. Pressure on the carotid sinus and digitalis and strophanthin failed to arrest the attack, which stopped on the fifth day after twenty grains of quinidine, the rate falling gradually from 220 to 194 as a result of quinidine, and then suddenly to 80. The signs of congestive failure quickly disappeared and within two days he felt quite well, but the changes in the cardiogram (Fig. 21) led us to keep him in hospital for three weeks, by which time the inversion of T I had disappeared. Because of these changes and because the paroxysms were ventricular and quickly led to congestive failure, his doctor was given a guarded prognosis. He kept well for two weeks and perhaps unwisely took tinct. dig., min. xx daily. His doctor wrote that as he was starting for hospital for his next routine visit he suddenly fell down dead ; there was no autopsy (Case 5).

The fifth patient started attacks when he was 24 and for the next 15 years they recurred each six or nine months, lasting from a few hours up to one or even two days. They were merely an inconvenience and he continued work as an engine driver.

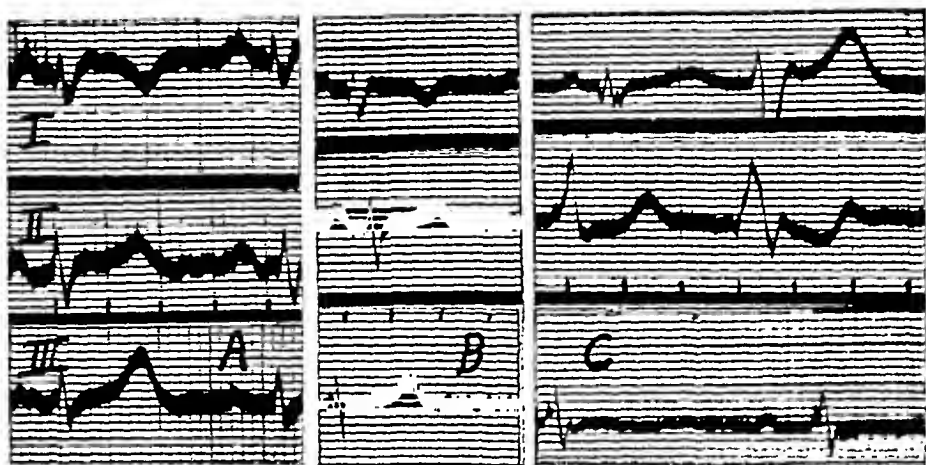


FIG. 21.—Changes simulating those of cardiac infarction, produced by a 10-day ventricular paroxysm ; (A) 2 days after, (B) 4 days after, and (C) 3 weeks after (Case 5).

In 1931, when he was 39, two attacks lasted 7 and 8 days, and for the first time he was ill enough to go to bed. Two months later he was admitted with congestive failure after 14 days of an attack which stopped when he had been given twenty minims of tincture of digitalis t.i.d. for three days. A cardiogram taken the next day when he seemed almost well showed some inversion of T in leads II and III, but ten days later these had gone, to be followed after a week by changes in the S-T intervals (Fig. 22).

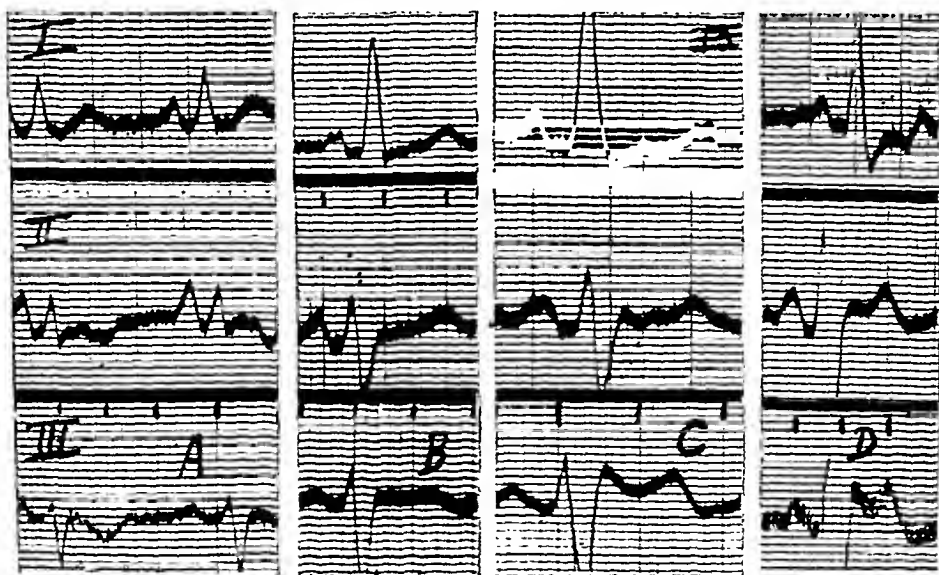


FIG. 22.—Changes after a 17-day paroxysm, simulating the changes after cardiac infarction ; (A) one day after, (B) eleven days after, (C) eighteen days after, and (D) four years after (Case 15).

Probably the inversion of T was due to the congestive failure and not to the digitalis or to coronary disease ; the findings at the autopsy described later and somewhat similar changes after other long paroxysms seem to justify this view.

Though he returned to work after some months he was never really well. In 1932 he had attacks of 8 and 14 days, and in 1933 nearly every month lasting about 4 days. In 1934 they generally lasted about 7 days and he was often away from work. Although there had been no more congestive failure he was able to do progressively less, and in 1935 had a pulmonary infarct during an attack. After this he gave up work and the attacks rarely lasted more than 4 or 5 hours. In 1936 his heart sounds were normal, his arteries soft, and his blood pressure 130/80; but an orthodiagram showed slight enlargement and the cardiogram (Fig. 22D) showed more depression of S-T in lead I than in 1933. Nothing else abnormal could be found; he had no attacks in hospital and was advised to increase his activity slowly and to take quinidine regularly; two months later he wrote that he had been better.

In 1937 he had another attack and after resting in bed three weeks he called in his doctor, but the paroxysm persisted, and there was progressive failure with jaundice and orthopnoea. On admission in the fifth week under the care of a colleague the heart rate was between 180 and 190, and he was dangerously ill. He was given 60 minims of tincture of digitalis, and during the night $\frac{1}{2}$ gr. morphia, but died next morning. At autopsy the heart weighed 450 grams (it seems unlikely that it was this weight the year before). There was no valvular disease, no signs of past syphilis, and very little atheroma of the aorta. The myocardium showed no scarring, and the coronary arteries were patent. There were 400 c.c. of slightly turbid fluid in the pericardium and the right pleural cavity contained a litre of blood-stained fluid. The lungs showed one very large and two smaller infarcts, as well as old scars. There was a large granular liver with nutmeg changes, and a firm dark spleen about twice the normal size (Case 15).

SUMMARY AND CONCLUSIONS

One hundred unselected cases of paroxysmal tachycardia have been studied and followed for some years. In 42 the diagnosis was confirmed by the electrocardiograph, in 30 by observation of an attack, and in 28 by the history alone. The criteria of diagnosis, when this has to be made on history, have been described; the sudden onset of palpitation being the most reliable single symptom. There may sometimes be difficulty in distinguishing paroxysmal flutter and tachycardia.

Of the 42 attacks with graphic records, 8 were ventricular and 34 supraventricular; 11 of the latter were nodal, but in many of the other 23 the site of origin could not be defined more precisely. Extrasystoles were observed between attacks in twenty-one, but were only of minor assistance in predicting the type of the attack. Ventricular paroxysms were very uncommon without serious heart disease.

There were 41 of these cases with heart disease, 19 rheumatic, 2 syphilitic, 8 hyperpætic, and 12 myocardial. There was no heart disease other than the arrhythmia in 59, though 4 of these had a goitre.

The rate was between 160 and 200 in nearly half; it was between 140 and 240 in 90 per cent., but occasionally outside this wide range. There was no great difference between the various ætiological groups. Nodal attacks tended to be a little slower and ventricular attacks were rather more often above 190, but even above this rate ventricular attacks formed a small minority.

Paroxysms are generally of short duration, lasting for hours rather than for days. In 61 the customary duration was less than two hours, and in

another 28 twelve hours or less. There were 4 where it was about twenty-four hours and only 7 where it was longer than this. But 18 others, making 29 in all, sometimes had attacks lasting more than one day, viz. over twenty-four hours, 10 cases ; two or three days, 8 cases ; up to seven days, 4 cases ; up to ten days, 5 cases ; and two to four weeks, 2 cases. One third, therefore, of our patients had some attacks lasting more than a day, 10 per cent. rarely, 10 per cent. often, and 10 per cent. habitually. Long attacks included an undue proportion of the ventricular paroxysms and were more common in those with myocardial disease.

Paroxysmal tachycardia is a symptom rather than a disease. In a minority of patients it accompanies serious heart disease, when, of course, the prognosis is grave. Such cases are nearly always under observation for their heart disease before the onset of paroxysms. Ventricular paroxysms form a fairly large proportion of this group and are rare otherwise. In most patients paroxysmal tachycardia is not in itself of any grave significance. It is due to reflex causes more often than to any primary change in the heart muscle. This applies not only to the majority whose hearts are otherwise normal but also to most of those with rheumatic heart disease and to some of those with other myocardial disease.

There is no close association between paroxysmal tachycardia and paroxysmal auricular fibrillation. In some of the rheumatic cases and less often in others paroxysms of fibrillation may alternate with or replace paroxysms of tachycardia. In the rheumatic cases established fibrillation then becomes a possibility in the near future.

The prognosis of paroxysmal tachycardia as regards life is therefore excellent, unless it is of the rare ventricular type, unless appearing relatively late in life it is the first indication of disease of the coronary arteries, or unless before the paroxysms have started there is already serious heart disease. Three of these patients have lived fifty years after the onset of their paroxysms, another 18 for more than twenty years, and another 26, making 47 per cent., for more than ten years, and most of these are still in good health. Paroxysmal tachycardia does not produce heart disease, even when it continues throughout life, though one possible exception to this statement has been quoted. In general the prognosis depends on the condition of the heart muscle and should be decided without reference to the paroxysms. There is no constant tendency for the paroxysms to get worse as life advances, and usually some form of treatment can be found which will reduce the frequency and the discomfort produced by the attacks.

We wish to express our thanks to Drs. F. W. Gordon and S. S. Suzman for their help with parts of the later follow-ups.

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CHANGES IN THE CHEST LEAD ELECTROCARDIOGRAM IN CORONARY THROMBOSIS

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This investigation was undertaken in order to show the sequence of changes and the variations occurring in the fourth lead of the electrocardiogram in cases of coronary thrombosis giving the T_1 or T_3 type of tracing. Particular attention was paid to the earliest abnormalities to occur and the last to disappear. Sixty-four clinical examples of coronary thrombosis were studied in which electrocardiographic abnormality confirming the diagnosis was present. No cases in which the tracings were doubtful or unconfirmatory were included. Twenty-four were acute cases examined electrocardiographically within a few hours to four days of the attack (eight within twelve hours). The criteria of abnormality in the standard leads were RS-T changes and T wave inversion occurring in the acute group over a period of a few days or weeks.

The chest lead used was that known as lead IV F. In this the right arm electrode is attached to the left leg and the left arm electrode is in contact with the outer edge of the apex beat. A normal tracing consists of an upright P wave, an upward initial wave R of good amplitude, a downward wave S, and an upward T wave. The S-T segment is either iso-electric or slightly elevated. Significant abnormalities in this chest lead electrocardiogram are R waves of less than 3 mm., elevation of more than 2 mm., and depression of more than 1 mm. of the RS-T segment, and inverted, diphasic, or very high-voltage T waves. The evidence for the pathological significance of these abnormalities has been given in a recent paper by Bourne and Courtenay Evans (1938).

ANALYSIS OF CASES

The cases were divided into two groups, according to whether the tracing was of the T_1 or T_3 type. A small third group consists of two cases with changes only in lead IV, and a single case of an anomalous type is placed in group four. These groups were subdivided so as to analyse the early changes in the acute cases, and the later changes in all cases.

GROUP I. CHANGES IN LEAD IV F IN THE T_1 TYPE OF ELECTROCARDIOGRAM. This group comprises 40 cases, 14 of which were seen in the acute stage.

A. *Early Stage*.—The initial deflection R_4 was absent in six, small in one, and

normal in seven of the 14 cases. Electrocardiograms were taken within eight hours of the thrombosis in three cases and the initial positive deflection was already absent; in one of these a tracing showed an absent R wave two hours after the occlusion. In three cases, four lead electrocardiograms had been taken before the coronary thrombosis occurred, and gave a normal R wave; after the thrombosis, in one case, a tracing taken on the fourth day showed an absent R wave; the R wave was not altered in the other two cases either

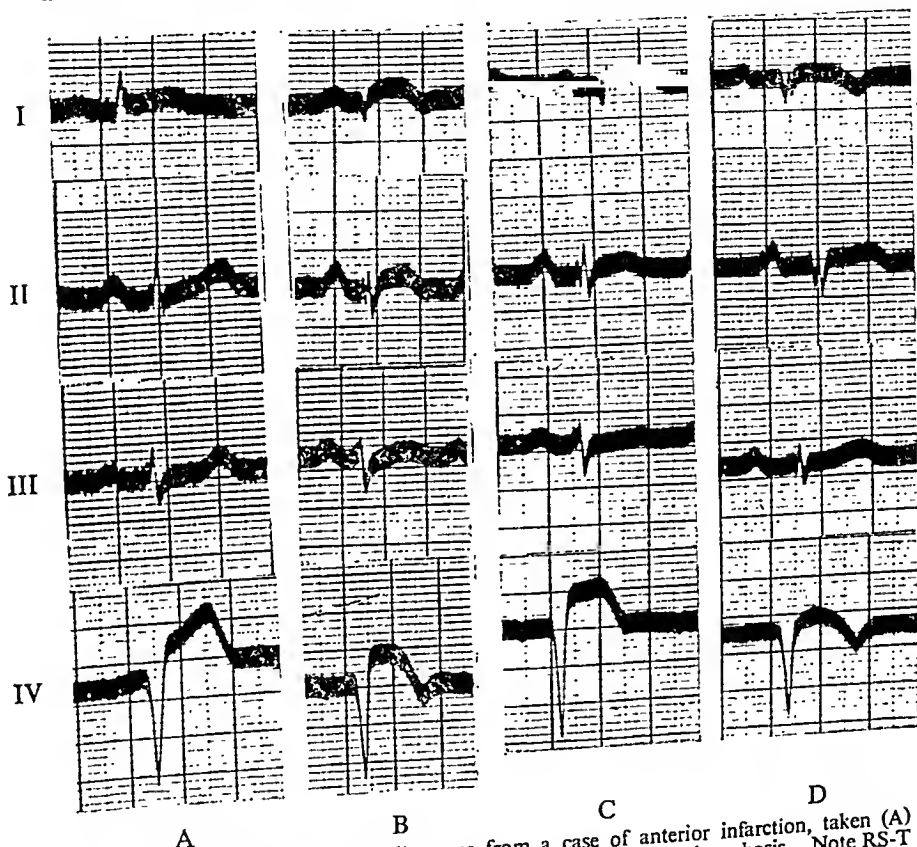


FIG. 1.—Serial T_1 type electrocardiograms from a case of anterior infarction, taken (A) 7 hours, (B) 4th day, (C) 5th day, (D) 11th day after coronary thrombosis. Note RS-T elevation and later inversion of T in leads I and IV; monophasic negative initial deflection in lead IV (i.e. absent R).

in the acute stage or later. No significant changes have been noted in the S wave, but splintering was present once.

The RS-T segment was elevated in eleven cases, the average elevation being 3 mm. and the extremes 1 to 8 mm. It was depressed in three cases, the average depression being 1 mm. Humping with an upward convexity and slurring of the RS-T segment occurred in eight, but was absent in six. This humping showed any time after the fourth day, and sometimes remained for several weeks, but was not as a rule a permanent change.

The T wave was upright in eight cases, but in seven of them it became

inverted later. In the other six, the T wave was inverted in the first tracing taken after the thrombosis. Inversion of the T wave was never seen earlier than the third day, and appeared most commonly on the fourth day.

In limb leads, RS-T elevation occurred in seven cases in lead I. In three cases, RS-T elevation in lead I or in leads I and II was the only abnormal finding, when lead IV showed an absent R wave and gross RS-T elevation. In

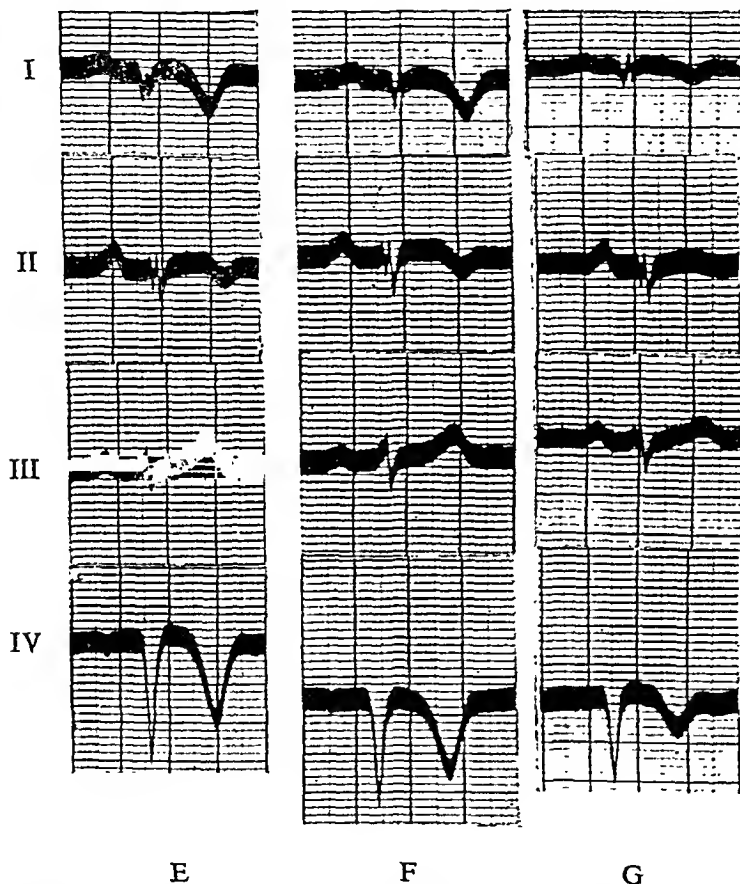


FIG. 2.—Later curves from same case as FIG. 1, taken (E) 21st day, (F) 32nd day, (G) 136th day after coronary thrombosis. Note disappearance of RS-T elevation; persistence of T inversion in leads I and IV, and transitory T inversion in lead II; absent R_4 persists.

one of these, T_1 and T_4 did not invert until the fourteenth day. T_4 tends to invert slightly earlier than T_1 ; in one case T_4 inverted on the fifth and T_1 on the twenty-third day.

B. Later Stage.—In lead IV, the R wave was absent in six of the fourteen acute cases; three of these I was able to follow up and the R wave was still absent in two, 175 and 306 days after the thrombosis respectively. The other had a normal R wave after 137 days. Many tracings were taken at varying

intervals. Of the three others, two died in the acute stage and the third, still with an absent R, was lost sight of after 29 days.

Twenty-six other cases with the T_1 type of cardiogram were examined ten days to five years after the thrombosis. Twelve had an absent R wave, one an R deflection of 1 mm., and thirteen a normal deflection. Of the thirteen with an absent or very small R, one only showed recovery in later tracings, and in that case it followed cardio-omentopexy; the remainder were unchanged.

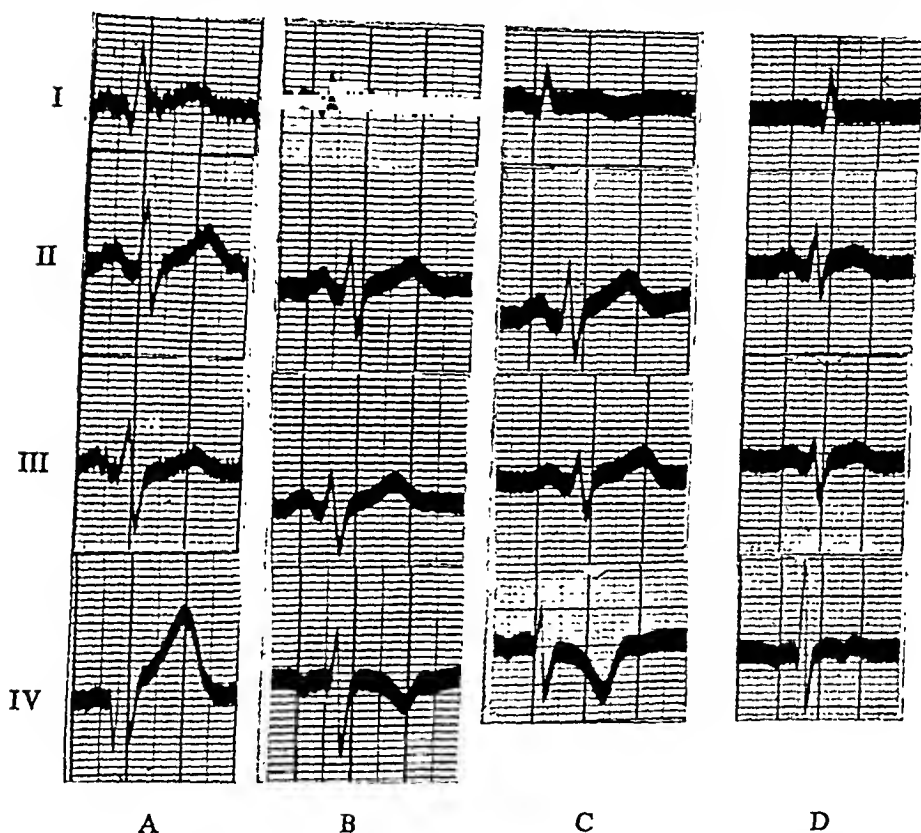


FIG. 3.—Serial T_1 type curves taken on (A) 1st day, (B) 5th day, (C) 29th day, and (D) 47th day after coronary thrombosis. Transient elevation of RS-T in leads I and IV; inversion of T_4 precedes inversion of T_1 . R_4 present throughout.

Most of these cases were repeatedly examined electrocardiographically for periods varying from five months to five years after the thrombosis.

Twenty-one of these forty cases with T_1 curves were followed up and seen on occasions five months to five years after coronary thrombosis. Analysis of lead IV showed notching of the QRS complex in three, W shaped QRS complexes in five, low-voltage QRS in one, and diphasic initial complex (QR) in three. The development of a diphasic initial complex (see Fig. 7 A) occurred a few months after the thrombosis in two cases, presenting at first an absent R wave and a large monophasic downward deflection. The S-T segment was

elevated in eight, iso-electric in eleven, and depressed in two. The T wave was inverted in twelve, diphasic in four, and normal in five. Three with diphasic T waves had formerly shown definite inversion. Of those with normal T waves, three were formerly inverted and return to normal occurred between the fourth and thirty-third week in one, between the eighth and twenty-fifth week in another, and between the fifteenth and thirtieth week in the other.

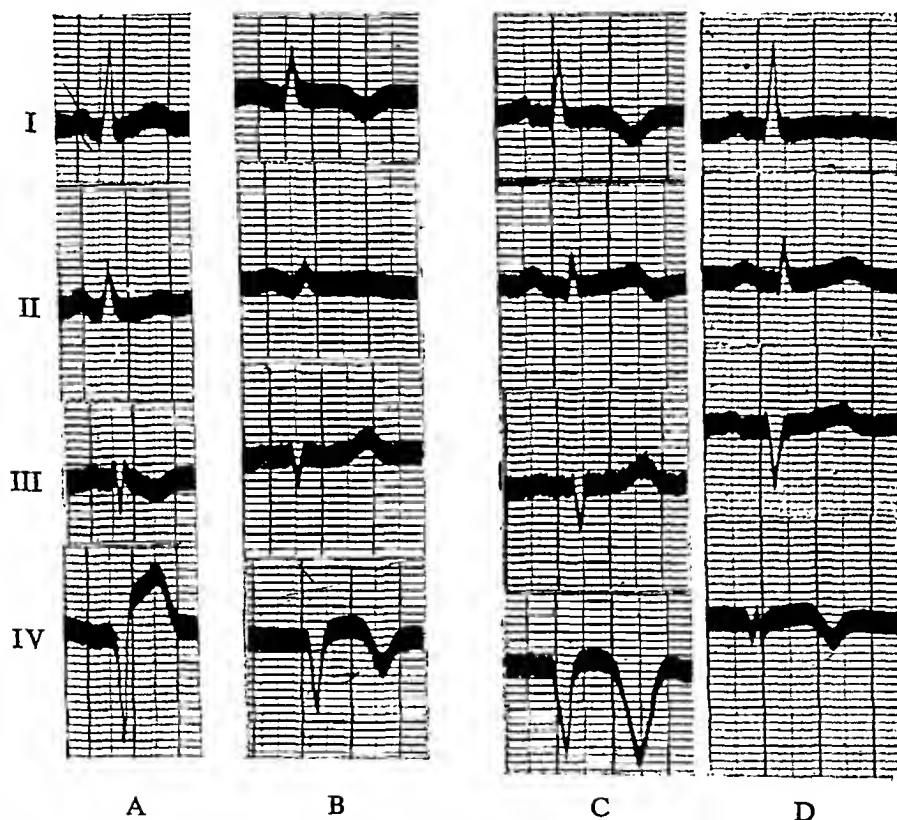


FIG. 4.— T_1 type curves in two cases of anterior infarction.

Case 1. (A) 6th day, showing earliest changes in lead IV only, i.e. Q-T elevation and absent R_4 . (B) 20th day, showing inversion of T_1 and T_4 with upright T_3 .
Case 2. (C) 39th day, showing inversion of T_1 and T_4 , with absent R_4 . (D) 291st day, T_1 inversion disappeared, but T_4 inversion persists.

In the limb leads T_1 remained inverted in nine, became diphasic in three, flat in four, and normal in five—inversion had been present in all. In the four cases which developed a flat T wave in lead I, T_4 remained abnormal; and in the five which changed to a normal T_1 , the T wave in lead IV remained abnormal in two.

GROUP II. CHANGES IN LEAD IV F IN THE T_3 TYPE OF ELECTROCARDIOGRAM.

A. Early Stage.—The initial wave R was normal in all of the eight cases; the QRS complex was W shaped in one. The RS-T wave was depressed in six

(average 3 mm., maximum 7 mm.) and iso-electric in two. The T wave was upright in seven, and diphasic in one. The diphasic T wave was transitory, lasting a few days, and returning to normal on the fourth day.

In the limb leads, the RS-T segment in leads II and III was elevated in seven on the third or fourth day. Two cases were examined electrocardiographically a few hours after the attack, one showed immediate RS-T elevation

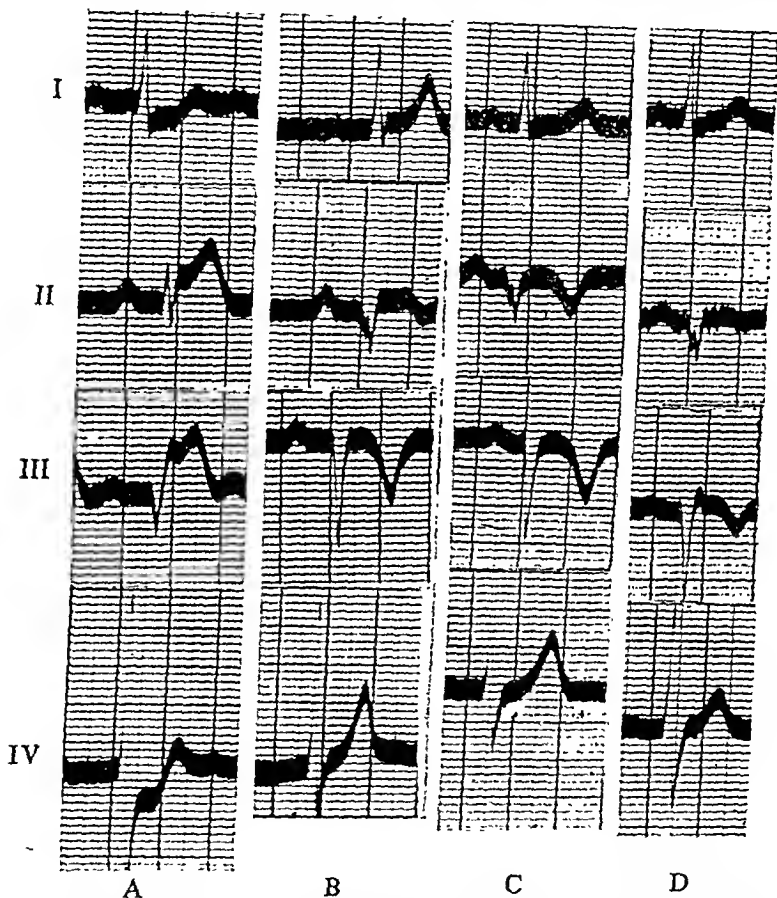


FIG. 5.—Serial T_3 type curves from a case of posterior infarction, taken (A) 4 hours, (B) 4th day, (C) 32nd day, (D) 172nd day after coronary thrombosis. Note elevation of RS-T in leads II and III and depression of R-T in leads I and IV, followed by inversion of T_2 and T_3 .

in leads II and III; the other remained iso-electric in the first tracing and gave the characteristic elevation on the fourth day. T wave inversion usually started on the third or fourth day, but one did not show inversion until the eighth. Six eventually had inversion of T_2 and T_3 ; two who died within the first seven days had no inversion. Post-mortem, one of these showed infarction of the posterior surface of the ventricles; there was no autopsy in the other. A Q wave was present in lead II in four cases, and there was an abnormally large Q in lead III in five cases.

B. Later Stage.—This is an analysis of eleven cases of coronary thrombosis with the T_3 type of electrocardiogram in which tracings were taken over four months or longer. In lead IV, the initial deflection R was normal in all cases. The RS-T segment was finally iso-electric in six, depressed in four, and elevated in one (formerly depressed). The T wave was finally upright in all eleven, and

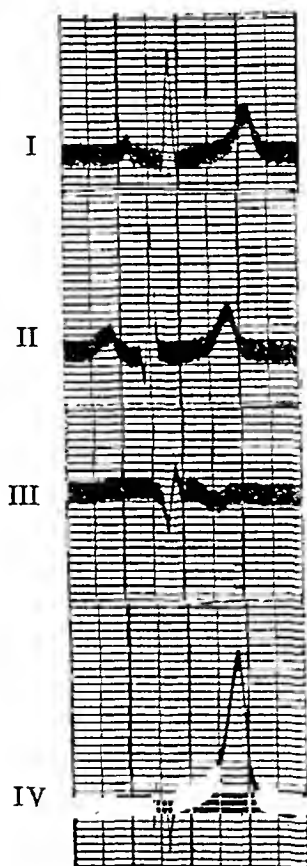


FIG. 6.— T_3 type curve 10 months after coronary thrombosis, showing Q_3 with slight inversion of T_3 . Note abnormally large T_4 (18 mm.).

in only one was there ever an inversion (14th day). The T wave became of large amplitude in two (19 mm.), returning to normal size in one. Humping of the RS-T segment with a downward convexity was seen in one case only. In limb leads, the Q wave in lead III remained large in six. T_3 remained inverted in seven and T_2 in three cases.

GROUP III. EVIDENCE OF CORONARY THROMBOSIS IN LEAD IV ONLY.

A. Early Stage.—In two cases, evidence of a recent coronary thrombosis was seen only in lead IV, there being no changes in the limb leads. The electrocardiogram showed T_4 inversion with subsequent return to normal in one, and

T_4 inversion with humping of the RS-T complex in the other. The clinical evidence of coronary thrombosis was very strong.

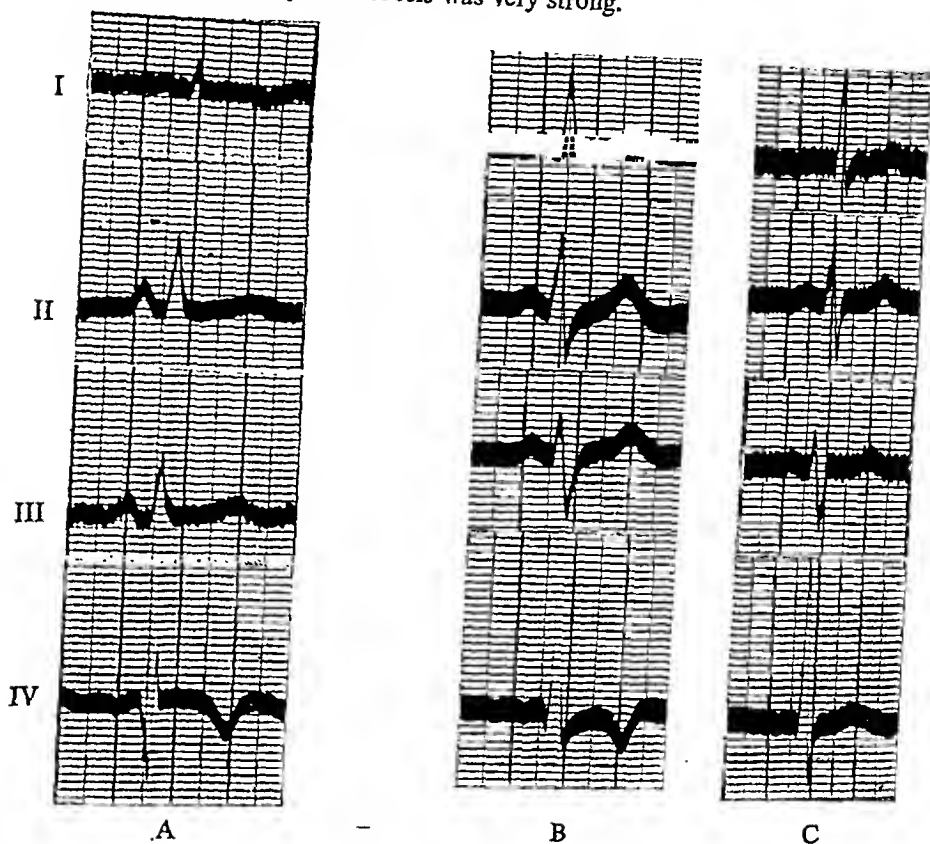


FIG. 7.—(A) T_1 type curve, 157 days after coronary thrombosis, showing diphasic initial complex (QR) in lead IV (previous curves showed monophasic negative initial complex). Curves taken on (B) 25th and (C) 49th day after coronary thrombosis, showing transitory inversion of T_4 and humped $R-T_4$ as only change.

B. Later Stage.—Four other cases, examined some time after the thrombosis, gave the only changes in lead IV, three by T wave inversion and one by an abnormally small R wave.

GROUP IV. ANOMALOUS CURVES AFTER CORONARY THROMBOSIS.

One acute case, which came to autopsy, showed elevation of $RS-T_4$, absent R_4 , elevation of $RS-T_1$, and later diphasic T_2 and T_3 . Auricular fibrillation, auricular flutter, and normal rhythm were present at different times. Post-mortem, a large infarct of the anterior and posterior surfaces of the ventricles.

POST-MORTEM EVIDENCE AND THE CHEST LEAD ELECTROCARDIOGRAM

Wood and Wolferth (1933) found, in experimental infarction in dogs, that depression of the RS-T segment occurred in anterior and elevation in posterior lesions. Using the standard lead IV, as in our cases, these findings would be reversed. Wood, Bellet, MacMillan, and Wolferth (1933) described thirty-one cases of acute coronary thrombosis, nineteen of which had anterior and twelve posterior infarction. The former had changes in the initial wave and in T_4 ; confirmation of the site of infarction was made by autopsy. Wood and Wolferth (1934), writing about abnormally large T waves in præcordial leads, describe such a case where autopsy showed an infarct on the anterior surface of the left ventricle. Willcox and Lovibond (1937) describe lead IV in six cases verified by autopsy. In three with posterior infarction, the correct diagnosis had been made from the limb electrocardiograms which were of the T_3 type. Of these, two had a normal lead IV, and the other an absent initial R, with slight elevation of S- T_4 , but the post-mortem showed also patchy fibrosis of the anterior surface of the left ventricle. Of the other three, one had an apical infarction and the electrocardiogram showed a large T_4 ; another had an anterior and apical infarct and the tracing gave a T_1 type of curve with an abnormal R_4 and inverted T_4 ; the last case revealed an antero-posterior infarct and the tracing showed depression of R-T in leads I and II, elevation in leads III, and IV, and an absent R_4 . Master, Dack, Kalter, and Jaffe (1937) describe the cardiograms of fifty cases examined post-mortem. Fifteen of these had anterior infarction with an absent initial R_4 in eleven, small R_4 in two, and normal R_4 in two. Thirteen had posterior infarction with a normal R wave in nine, small in four, and absent in one; the latter also had an old partial occlusion of the left anterior descending coronary branch. In nineteen cases anterior and posterior infarctions were present; the R wave was absent in four, and small in one-half of the cases. Two cases had infarction of the lateral wall of the left ventricle and one case infarction of the septum; the QRS complex was normal in all three. Master only referred to the initial wave changes, not to the T waves.

In our series there were two autopsies. One of these showed recent infarction of the posterior surface of the left ventricle with sclerosis of the descending branch of the right coronary artery, but no arterial thrombosis. The tracing taken three days before death, on the fifth day, had elevation of the R-T segment in leads II and III, slight enlargement of Q_3 , and humping of S-T in lead III. Lead IV was normal. The other case had extensive recent infarction of the whole of the left aspect of the interventricular septum and of adjacent parts of the anterior and posterior surfaces of the left ventricle; the right coronary artery showed patchy areas of atheroma, and the left coronary at the commencement of the anterior descending branch was filled by adherent ante-mortem clot. The electrocardiogram as already described (Group IV) was anomalous.

Left Lateral Infarction.—Wood, Wolferth, and Bellet (1938) have described a type of electrocardiogram which they state is characteristic of left lateral

infarction. They produce post-mortem evidence and suggest that usually the circumflex branch of the left-coronary artery is occluded. The characteristics of the tracing are depression of RS-T in leads I, II, and IV, with a diphasic or inverted T wave in lead I, and an inverted T wave in lead IV. Auricular fibrillation is a common association. Electrocardiographic features may subside very rapidly, and after healing of the infarct all the changes may disappear from the tracing.

Three of my acute cases from Group I, with a T_1 type of electrocardiogram, had depression of RS- T_4 , maximum 3 mm., and in two the RS-T segment in lead I was slightly depressed also. The R wave was present in all three. These are possible examples of left lateral infarction.

SUMMARY AND CONCLUSIONS

In the T_1 type of electrocardiogram after coronary thrombosis, the changes in lead IV occur in the following sequence. The initial wave R disappears immediately in half the cases, and elevation of the R-T segment, 3 mm. above the iso-electric level, occurs at the same time in three quarters of the cases. The T wave becomes inverted on the third or fourth day, synchronous with or slightly earlier than inversion of T_1 , and sometimes many days earlier. At the same, time, the R-T elevation diminishes and, in half the cases, changes any time after the fourth day into a humped upward convexity with broad slurring of the curved portion. Return of RS-T to normal, with disappearance of the humping, occurs after several weeks. T wave inversion disappears in half the cases between the third and sixth month, but in behalf the cases it persists. The initial wave R, when once absent, usually tends to remain absent; the initial complex in these cases sometimes becomes diphasic (QR).

In the T_3 type of electrocardiogram, RS-T is depressed 3 mm. below the iso-electric level, returning to normal within a few days in two thirds of the cases. The initial R wave is present, the S wave is often small, and sometimes a W shaped complex is seen. Later, humping of the S-T segment with a downward convexity occurs in a few cases, but is not common. The T wave is upright and tends to increase in amplitude; it may attain 13-19 mm. in the second or third weeks. As a rule the changes in lead IV, after the initial RS-T depression has passed, are slight and not very helpful in diagnosis.

Post-mortem evidence suggests that T_1 and T_4 inversion, and absent R_4 with elevation of RS-T in leads I, II, and IV indicate an anterior infarction, and that T_2 and T_3 inversion with depression of R- T_4 indicate a posterior infarct. Where absence of R_4 and T_4 inversion are associated with inversion of T_2 and T_3 , the evidence points to infarction of both anterior and posterior ventricular walls. The third type of occlusion, involving the left circumflex artery and causing left lateral infarction, shows RS-T depression in leads I, II, and IV, with inversion of T in leads I, II, and IV. These changes are often of a transitory nature and may be associated with auricular fibrillation.

I am indebted to Dr. Geoffrey Bourne for help and advice in carrying out this work, and I wish to acknowledge a personal grant from the Medical Research Council.

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TRAUMATIC ANEURYSM OF THE LEFT VENTRICLE

BY

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Although aneurysm of the heart is still thought to be a somewhat rare and unusual pathological condition, recent work shows that it occurs not infrequently after coronary occlusion and infarction. Parkinson, Bedford, and Thompson (1938) estimate that it occurs in 9 per cent. of cases of cardiac infarction examined at necropsy. In the absence of coronary disease, aneurysm of the heart appears to be exceedingly rare; and trauma as an exciting cause is seldom referred to in papers on the subject. Warburg (1938) in a recent monograph has collected, from papers and reports dating back to the year 1676, 197 cases of cardiac lesions due to non-penetrating injuries, but of these only two or three appear to be instances of traumatic aneurysm of the heart.

The case recorded here is one of traumatic aneurysm of the left ventricle, due to a non-penetrating injury to the thorax. Although the diagnosis was not made during life, the case presents some interesting points clinically and medico-legally.

He was a man, aged 59 years, a non-smoker and life abstainer. While driving a motor car he was involved in a head-on collision with another car on July 12, 1936. Immediately after the accident he noticed pain in his knees only. He was able to help some other people who had been injured, and later with assistance he changed the wheel of his car. Following this he experienced sudden severe pain in the region of his heart and became short of breath. An injection of morphia was given, and as a condition of shock still continued, he was taken by car to a neighbouring town. On arrival there he was seen by a doctor, and next day was admitted to the local hospital, as the præcordial pain had again become severe and was accompanied by marked dyspnœa. A tentative diagnosis of pericarditis was made. While in hospital he developed a left-sided pleurisy, and an X-ray photograph is said to have revealed a fracture of one of the left lower ribs near the vertebral junction. He was discharged from hospital on July 23 and returned to his own home by train.

On July 30 he was seen by a surgeon, who reported as follows: "There were tender points over the left costal cartilages and over the xiphisternum, and

over the eleventh rib at the back. The patient showed abnormal nervousness and increased reflexes. He breathed with short gasps and could not take a deep breath; his pulse rate was 98. In my opinion the patient has suffered a crushing injury to the chest, probably due to striking against the steering wheel at the moment of collision. The crush has injured the costo-condral and costo-sternal junctions over the fifth to seventh ribs, which interfere with normal breathing. He will be confined to his house for at least a month, but may be able to do some light work in three months' time. His expectation of life has been adversely affected."

On August 6 he was seen by the present writer on account of an acute heart attack on the previous evening. On examination he was in great distress from severe shortness of breath, with a feeling of constriction and pain in the chest. The heart was rapid and irregular (auricular fibrillation). The blood pressure was slightly raised and there was distinct præcordial tenderness. On careful inquiry there was no history of any significant illness previous to the accident and nothing to suggest that there ever had been any symptoms of cardiac disability: With complete rest, sedatives, and digitalis the cardiac condition seemed to undergo improvement. As the heart rate became steadier the sounds became of a "tic tac" quality, and the breathing, though less embarrassed, always seemed to occur in short, sharp "whiffs." From time to time he experienced attacks of pain like angina of varying severity, and morphia had to be given on several occasions. Throughout his illness he was nervous and apprehensive, and there was always some slight tenderness over the præcordium.

At the end of August he was allowed up for a short time, but as this caused respiratory distress he was ordered back to bed. After a further period of rest in bed about five weeks he was again allowed up and arrangements were made for electrocardiographic and X-ray examinations. Unfortunately these investigations were not carried out, as he developed a left-sided pleural effusion early in October. On October 18 he died suddenly in an acute heart attack.

Post-mortem Examination (Prof. J. McGrath).—The body was that of a well-built man, of healthy appearance, with a moderate amount of fat. There was no evidence of bruising on the front of the chest. On opening the chest, the left pleural cavity was found to be almost completely filled with a large quantity of clear, straw-coloured fluid. The lower lobe of the left lung was entirely collapsed, as was also the lower portion of the upper lobe. The left lung itself, except for the above findings, appeared normal. There was the usual emphysema for a man of his age. The right lung showed old adherent pleurisy.

A moderate amount of fat surrounded the heart. The pericardium externally appeared thickened at the apex. On opening, it contained a small amount of fluid. At the apex over an area the size of a five-shilling piece there was fibrous adherent pericarditis. The heart muscle was thinned out under the area and formed a cardiac ventricular aneurysm. The heart was enlarged, especially the left ventricle, this enlargement being due to dilatation of the cavity with thinning of the muscle. The muscle (especially the apex) was permeated with fibrous tissue, and there was some endocarditis with adherent blood clot over an area the size of a half-crown. The aortic and mitral valves appeared

efficient, but there was some simple atheroma. It did not seem possible that these valves could be the cause of the ventricular condition. There was no occlusion of the coronary arteries.

Examination of the ribs did not show any site of fracture in the bones. The

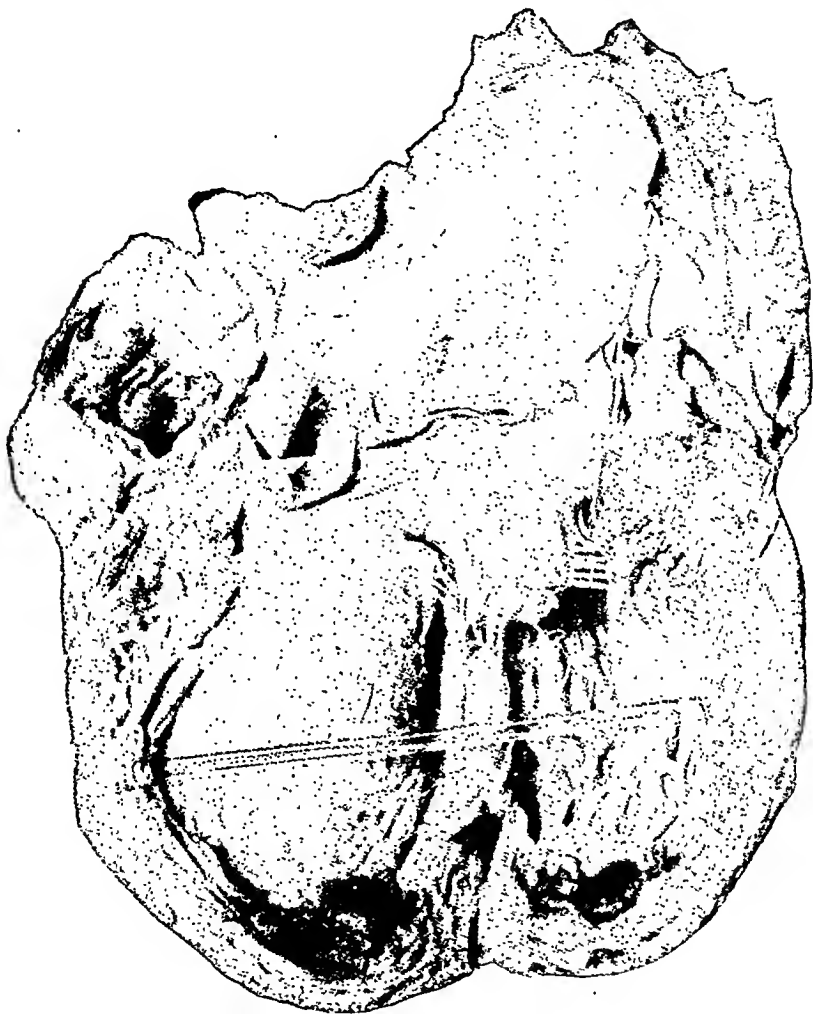


Figure illustrating traumatic aneurysm of the left ventricle, with apical myocardial fibrosis and localized endocardial thrombosis.

cartilaginous portion of the fifth, sixth, and seventh ribs over the heart apex was irregular and appeared to have been depressed slightly. There was a localized patch of pleurisy on the left parietal pleura posteriorly between the eleventh and twelfth ribs, in size about one and three-quarter inches in diameter. This patch of pleurisy was raised and reddish-yellow, and covered with granul-

ation tissue ; it was evidently the cause of the pleural effusion, and was in direct line from back to front with the pericardial adhesion. A search was made for a rib fracture in the neighbourhood of this patch of pleurisy, but it could not be found.

Death was due to cardiac failure. This cardiac failure was caused by degeneration of the heart muscle with consequent dilatation (aneurysm) and endocarditis of the left ventricle. The degeneration seemed to have spread from the pericardial adhesions. These adhesions and the localized pleurisy at the back were in direct line with the abnormality of the costal cartilages in front, and could have been the result of an impact on the chest. From the history of the case, the injuries sustained in the motor car accident were the original cause of the sequence of events that led to his death. There was, however, old-standing pleurisy on the right side, and some of the heart disease possibly antedated the accident.

COMMENTS

(1) *Clinical Aspects.*—Although this patient was obviously suffering from a grave cardiac condition throughout his illness, the true nature of the lesion was not fully appreciated, nor was a sudden death anticipated. Taken generally, the clinical picture resembled that of coronary thrombosis, except that a sub-acute form of "status anginosus" seemed to have persisted intermittently for several weeks. The constant tenderness over the præcordial area appeared to indicate damage to the underlying cardiac musculature.

An interesting point in the clinical history was the delay in the onset of cardiac symptoms after the accident. It appears, however, that a latent period is not an unusual finding ; for instance, Elkin (1935) cites a case of cardiac contusion following a motor-car collision, where the patient walked for a distance of 50 yards from the scene of the accident before he experienced shortness of breath. Beck (1935) also states that symptoms of cardiac injury may be delayed for hours and sometimes for days. Presumably in the present case the patient's heart was actually contused at the time of the impact ; but symptoms did not become manifest until the area of contusion, owing to extravasation of blood in the muscle, simulated a myocardial infarct.

The occurrence of auricular fibrillation following direct trauma to the chest wall has been observed by Barber (1938), White (1937), the Khans (1928), and others, and therefore it cannot be regarded as an unusual complication. The development of "tic tac" heart sounds in cardiac trauma has been shown by Bright and Beck (1935) to occur experimentally in dogs, and the same writers have observed a similar phenomenon in human beings following non-penetrating injuries of the thorax. A very striking feature in the present case was the peculiar short "whiffing" type of breathing, which may perhaps have been of some diagnostic significance though at the time it was unaccounted for. The state of anxiety and nervousness shown by the patient was seldom absent and on several occasions amounted to a veritable "angor animi."

As no electrocardiogram or X-ray photograph was taken, one can only

speculate on the possible findings. The post-mortem lesion suggests that during life an electrocardiographic tracing might have shown inversion of T in lead I, indicative of damage to the anterior and apical portion of the left ventricle, which might have been misinterpreted as pointing to a true coronary thrombosis. On the criteria given by Parkinson, Bedford, and Thompson (1938) it is unlikely that an X-ray photograph would have disclosed the presence of an aneurysm, for the heart as it lay *in situ* did not show marked bulging of the ventricular wall.

(2) *Medico-legal Aspects*.—Fortunately for most of those concerned, the case was settled out of court with substantial monetary compensation to the dependants of the deceased. There is no doubt that had the case come to trial certain difficulties might have arisen. The history of an injury in a previously healthy man would of course have carried considerable weight in a court of law, but it would have been impossible, without the post-mortem findings, to state definitely that no coronary disease had existed previously. If some coronary disease had been disclosed at the post-mortem examination it would have been rather difficult to decide how far the injury had aggravated a pre-existing disease so as to cause fatal outcome. Should the patient have survived, the question of assessing compensation might have proved even more difficult.

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ANGINA PECTORIS FOLLOWING A CRUSHING ACCIDENT

BY

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Trauma, it is generally agreed, plays an unimportant part in the ætiology of heart disease, but occasionally, as in the preceding paper by O'Farrell (1939), an injury provides an interesting and unusual problem. In the case that follows, the absence of any electrocardiograms soon after the accident makes the evidence incomplete, but it is the best instance seen by the writer of an injury producing a picture very similar to that of a cardiac infarct.

A man of 47 years felt very fit and was able to do heavy work as a furniture-remover without any symptoms ; he had actually won a race of a hundred yards at some local sports four years before although he then weighed 14 stone. He gave no history of any previous illnesses.

One afternoon when he was unloading furniture, a fireplace surround weighing 3 cwt. slipped from the van and fell against his chest. It struck him just to the left of the mid line, inside and above the apex beat, and pushed him backwards, but a wall behind him prevented him from falling. He was imprisoned in this position for five or ten minutes, crushed between the wall and the fireplace surround. The pain was not severe ; in fact, he said that he felt nothing that could really be called pain. When he was released he felt shocked and shaky ; he sat down and rested for an hour, but still does not remember feeling any special pain. It was then an hour before work finished for the day, and he carried on for this time feeling fairly all right, but naturally not doing anything heavy.

When he had finished work and locked up, two hours after the accident, he started to walk home. After about 200 yards he had very acute pain in the middle of the sternum, which immediately made him stop until it passed off. This was the first real pain he had experienced, and it was accompanied by dyspnœa ; it recurred five or six times on his way home. He tried to do some work the next few days but could hardly do anything, and the pain got worse, i.e. more easily provoked, even on walking about slowly. After four days it seemed as bad as ever, so his doctor sent him to bed for two weeks. There had been no attack of pain that was outstanding in its length or severity, but all were very severe and he could hardly say if they were worse the first evening or during the next four days. This rest at once stopped the attacks of pain, but

they returned again when he started to get up and about. He was sent to hospital and was advised to rest for three months ; he did not have an X-ray examination, but there seems to have been nothing to suggest a fractured rib. He spent this three months quietly at home and was free from pain so long as he did not try to do much.

He was first seen by me at the National Hospital for Diseases of the Heart in October 1932, four months after the accident. He felt he was improving, but complained that on any exertion, especially on walking quickly, he had a sharp pain, which started near the left costal margin, passed up the middle of the sternum to the throat, and made him stop until relief came in two or three minutes. There was some dyspnœa with the pain, but both were less severe than at first. The cardio-vascular system cannot have been normal before his accident, as the aorta was rather widened and atheromatous and the retinal arteries were thickened ; the heart was probably a little enlarged, the maximum transverse diameter being 12.5 cm. in a chest of 24.5 cm., although its rather horizontal position made the determination of slight enlargement difficult. The only other abnormal physical signs found were a blood pressure of 150/100 mm. and an electrocardiogram showing a flat T 2 and a slightly inverted T 3.

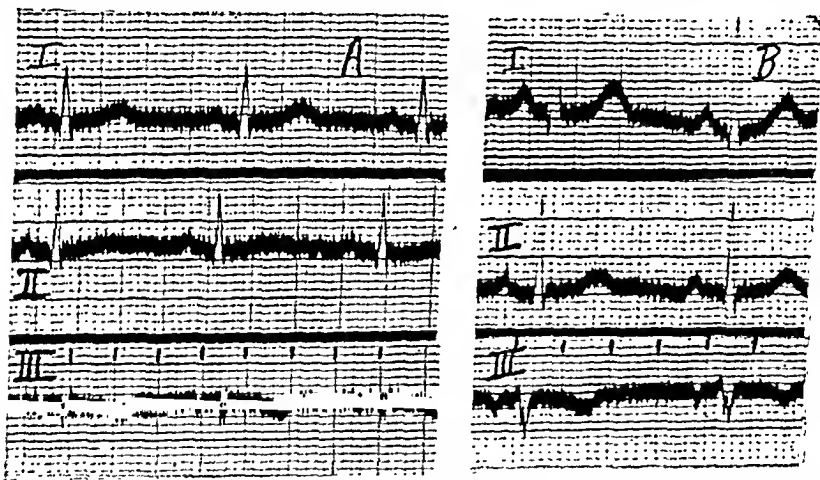


FIG. 1.—Electrocardiograms taken (A) four months and (B) five years after the accident. The improvement in the T waves, in spite of the heart having increased in size, suggests that the T waves may have been even flatter or inverted just after the accident.

After six weeks he was allowed to resume light work, as though the pain still returned if he exerted himself too much, he felt quite well when he did not do anything strenuous. The blood pressure, which had been 150/100 mm., had fallen to 130/90 mm., so probably some of the rise on the first occasion was temporary and due to excitement. He was fortunately an old and valued servant of the firm, so was given very easy work wrapping up and despatching parcels.

He was not seen again till 1937—after an interval of five years. He felt all right if he led a quiet life, but still got pain on any exertion. This started in the

epigastrium and passed up to the throat with a sensation of choking and made him stop, until it had passed off after he had rested for a few minutes. The pain was more likely to come on walking than at work ; but ever since the accident he had continued to do the same easy work, which did not involve any heavy exertion. On examination his heart had increased 2 cm. in size to 14.5 cm., but the increase in weight, from thirteen to fourteen and a half stone, might have been partly responsible. The second sound was accentuated in the aorta area, and the blood pressure was 160/100–105 mm., a little higher than in 1932. His electrocardiogram showed large upright T waves in leads I and II, with some inversion of T in lead III. It is unfortunate that no complete series of curves had been taken in the first few weeks after the accident, as they might have proved the presence or absence of an actual infarct ; but in 1932, four months after his accident, T in lead II had been almost flat and T in lead I smaller, so it seems likely that there had been earlier changes similar to those found after cardiac infarction.

At this stage the case was taken to court under the Workmen's Compensation Act and he was awarded £500 and additional payment for the time he had been off work ; he was allowed to continue the light work he had been performing for five years. The opinion expressed by the writer was that an actual thrombosis in a coronary artery or other localized damage in the heart muscle had resulted from the accident and within a short time of it ; and that his anginal pain was due to this cause. It was admitted that his cardiovascular system might not have been normal before the accident, but he had been able to do heavy work without any cardiac symptoms.

After another two years (1939) his condition has not changed greatly. The T waves in his electrocardiogram have become a little flatter, though perhaps the pain is less easily provoked. He is still doing the same easy work. There has been no further increase in the size of his heart.

Barber (1938) has reported twenty instances of heart disease that he attributes to trauma or strain, seen in the course of thirty years' practice. In two of these, both elderly men, anginal pain followed an injury ; one had a fracture of the sternum where he was struck by the shaft of a cart, and the other had bruised his ribs from jumping on a moving cart. Both had to rest after the accident and the anginal pain was first noticed when they started walking three and two weeks respectively after their accidents. It is not clear how long the pain persisted. He quotes a third example reported by Fraser (1929).

SUMMARY

A man who was leading an active life and doing heavy manual work without any cardiac symptoms, developed sternal pain within two hours of a crushing accident ; and this pain continued afterwards and was associated with some progressive increase in the size of his heart. There seems no doubt that the actual damage done to the heart at the time he was crushed was responsible for these symptoms and signs.

The commonest severe injury to the heart in crushing accidents is rupture of muscle fibres, sometimes through the whole thickness of the muscle wall; and in this case rupture of muscle fibres and extravasation of blood might account for all that was found without an actual thrombosis. But the fact that typical anginal pain, which he had never experienced before, occurred so soon and persisted for so long after the accident makes it likely that an actual thrombosis was produced while he was imprisoned, and that as soon as he started to walk after this he felt anginal pain. Alternatively, an injury or contusion of the artery at the time he was crushed might have been followed by an actual thrombosis two hours later, when he first felt severe pain. In either case, his symptoms were just those that would be expected after a cardiac infarct, and he seemed to have been in perfect health up to the time of the accident.

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A CASE OF MASSIVE HÆMOPERICARDIUM WITH RECOVERY AFTER PARACENTESIS

BY

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A young woman, aged 20 years, was admitted to the General Hospital, Colombo, under my care on June 4, 1938, with a history of having received a blow with a fist on the front of her chest the previous day. As regards her previous history, she had had pneumonia four years before and some attacks of malarial fever. She had not been in good health during the preceding six months, and attributed this to a recent pregnancy which had ended in an abortion at the fourth month.

On admission she was pale and dyspnoëic. Her pulse rate was 100 and low in volume and tension. The respiration rate was 48 per minute. The lungs were resonant and the air entry was normal, with no adventitious sounds. The heart sounds were feeble and muffled. The apex beat was not palpable. Percussion of the heart revealed a large area of dullness, extending from the left axillary line to the right mid-clavicular line. A hæmopericardium was suspected. There were no injuries to the sternum or ribs. The liver and spleen were not enlarged. There was an enlarged lymphatic gland in the left axilla. This gland was excised subsequently and the pathologist reported that it was one of tuberculous adenitis with caseation. A radiogram (Fig. 1) was taken, and the radiologist reported that the appearances suggested a large pericardial effusion. The diagnosis of hæmopericardium was confirmed by Dr. H. O. Gunewardene also, who kindly saw the case in consultation.

On the following day the condition of the patient was slightly worse. There were periodical exacerbations of dyspnoëa while she remained propped up in bed. An ice-bag to the chest and morphia gave her some relief. On the third day her pulse rate was 120, and dyspnoëa continued. Paracentesis was decided upon and performed, and six ounces of dark sanguineous fluid was aspirated. Dr. de Saram, the pathologist, reported that the aspirated fluid was blood and that it contained no organisms and no pus cells. The patient felt slightly relieved after aspiration, and it was followed by a gradual slowing down of the pulse and respiratory rates. Her temperature, which was slightly raised at first, became rather higher for four or five days and then began to subside (Fig. 2).



FIG. 1.—Radiogram taken shortly after admission to hospital showing a large pericardial effusion and a small hydrothorax at the left base.

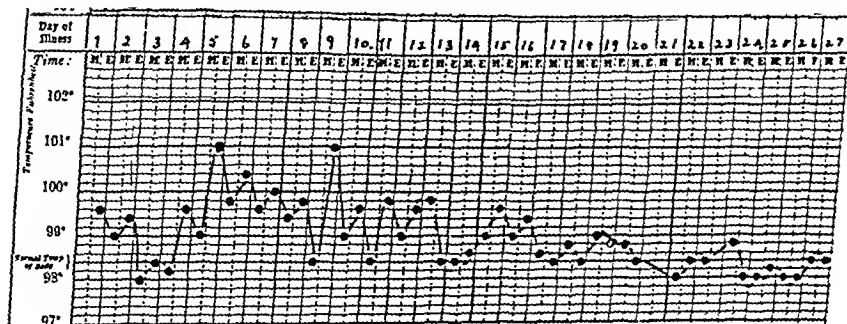


FIG. 2.—Chart of morning and evening temperatures.

On the advice of the Senior Physician, Dr. J. R. Blaze, nothing further was done, apart from keeping her on sedatives. The area of cardiac dullness diminished from day to day and in a week it was nearly normal (Fig. 3). At

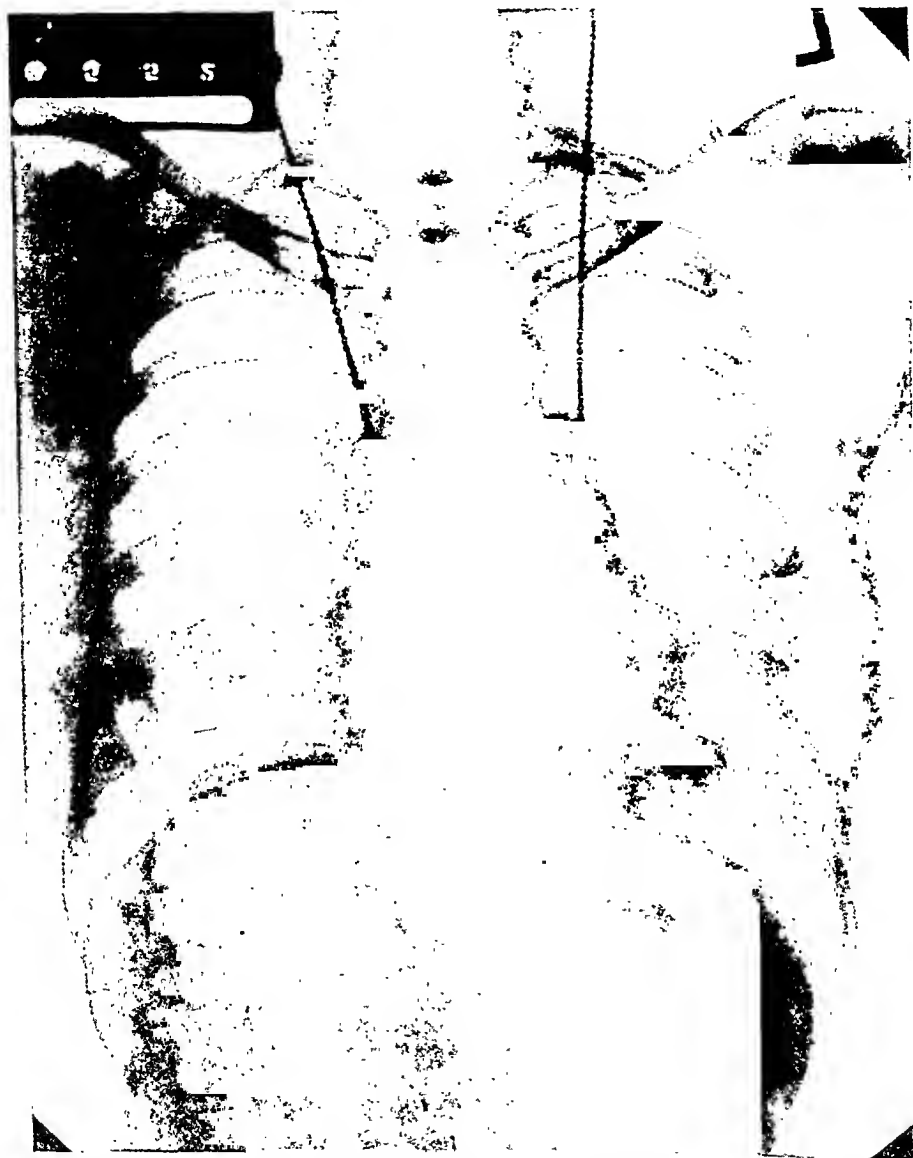


FIG. 3.—Teleradiogram (two metres) taken about a week after aspiration.

the end of a fortnight it was quite normal, and this was confirmed by a two-metre radiogram (Fig. 4).

The patient left hospital on August 17 completely cured, with a normal pulse rate and no murmurs. She was seen three months later in good health and was quite able to attend to her household duties.

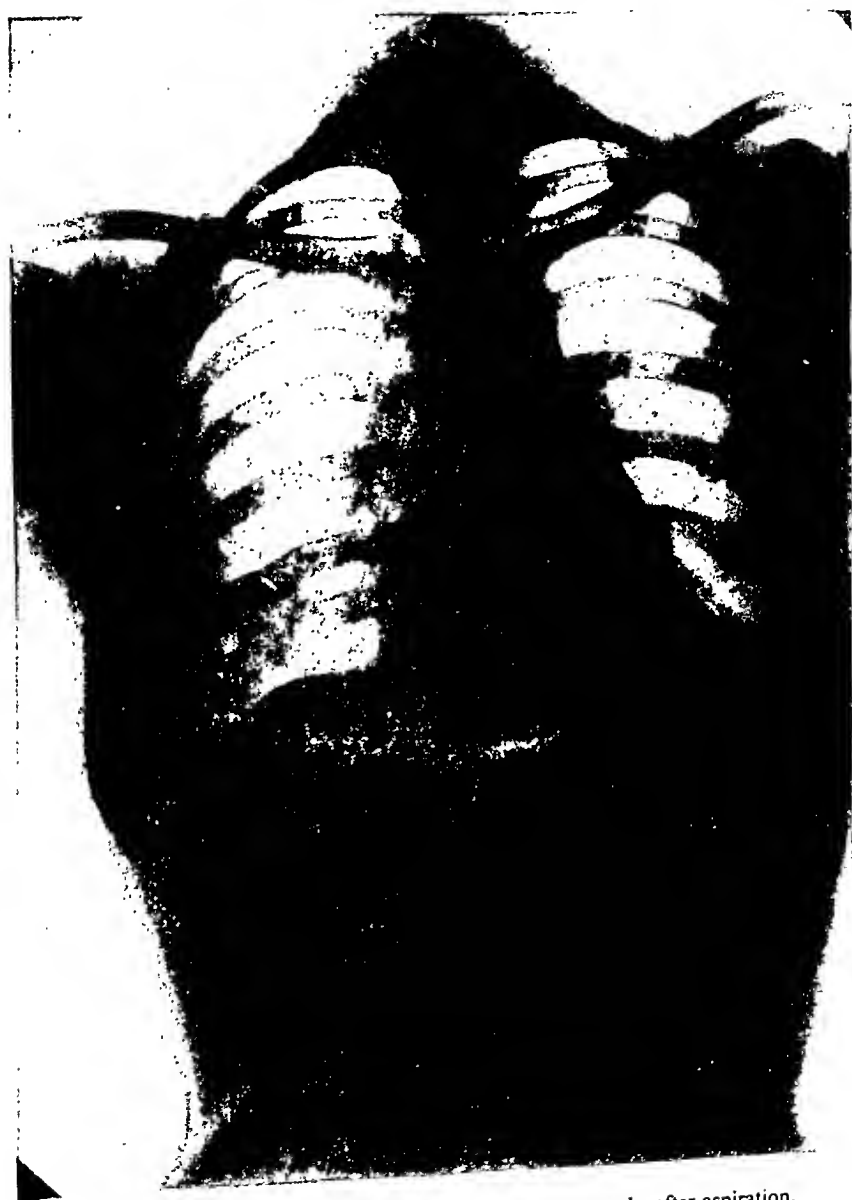


FIG. 4.—Teleradiogram (two metres) taken about two weeks after aspiration.

DISCUSSION

The case is of unusual interest because a large hæmopericardium or a large hæmorrhagic pericardial effusion had been caused by a blow which produced no external injuries.

The rapid absorption of a considerable amount of blood in the pericardial sac, determined clinically by the reduction of the extensive area of dullness almost to the normal limits of cardiac dullness within a week after the aspiration, strongly suggests that the pericardium was in a previously healthy condition. The presence of a tuberculous gland may suggest the possibility of a tubercular pericardium, but the complete return to its normal limits as shown in the second two-metre radiogram (Fig. 4) puts this possibility out of court.

The source of bleeding is a matter of conjecture. There was no evidence of hæmophilia or other blood disease.

The pathologist's report on her blood was as follows :—

Bleeding time : $2\frac{3}{4}$ minutes.

Coagulation time : 3 minutes.

White blood corpuscles : 8,800 per c.mm.

Red blood corpuscles : 3,430,000 per c.mm.

Differential count : Polymorphs, 74 per cent.

Lymphocytes, 23 per cent.

Eosinophils, 3 per cent.

Judging from the steadily progressive nature of the bleeding it was reasonable to surmise that there was bruising of the parietal and visceral layers of the pericardium. There might have been a sub-serous contusion of the musculature of the heart. The latter is, however, unlikely owing to the absence of any effects afterwards.

The successful treatment of this case by aspiration shows that operative treatment is not essential in every case of traumatic hæmopericardium, and that the prognosis is sometimes better than that suggested by Price (1937). Natural arrest of bleeding probably takes place when the intra-pericardial pressure reaches a certain point, and it is therefore probably wise to temporize with sedatives and an ice-bag to the chest in the hope of arresting hæmorrhage. If cardiac distress is nevertheless acute and progressive, operative treatment would be necessary.

SUMMARY

1. A case of traumatic hæmopericardium without external injuries is reported.
2. Treatment by aspiration was successfully carried out.

Note by Editor. Gunewardene (1934) reported a case of a boy whose chest was crushed by a bullock cart. He returned to school and was able to play games without any pain or other symptoms. Eleven days later he com-

plained of some præcordial pain and fell down dead. There was a recent rupture of the left ventricle and it was thought to be a tear in the previously damaged muscle. Barber (1938) reported two somewhat similar cases where death took place after 4 weeks and after 6 weeks respectively.

Mayer (1936) reported seven cases seen in hospital in a period of two years. Most of them were stab wounds: in three the bleeding came from stab wounds of the left ventricle, and in three there was thought to be an anterior mediastinal hæmatoma. Five of these cases recovered and two recovered without surgical treatment, as in the case reported here.

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ALCOHOLIC BERI-BERI HEART

BY

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Heart failure due to vitamin deficiency has not hitherto attracted much attention in this country. A single case was reported recently by Price (1938) and another by Yudkin (1938). The case that follows illustrates certain features characteristic of the condition.

CASE REPORT

A man, aged 36, was admitted to the Manchester Royal Infirmary on November 11, 1938, with acute heart failure. The distribution of the œdema was unusual and, in certain respects, resembled that of renal rather than that of cardiac insufficiency. The face was puffy, the eyelids swollen; there was massive œdema of the legs extending to the thighs; the penis and scrotum were enormously swollen; the abdomen was distended and contained free fluid; moist sounds were present in the lungs; there was slight engorgement of the veins of the neck and the liver was palpable.

Swelling of the ankles, which was greatest in the morning and diminished towards evening, had first been noticed only two weeks previously, and shortness of breath on exertion had been present for only ten days. Three months prior to admission the patient had felt perfectly fit, but his friends had remarked on the fact that he had required to pass water surprisingly seldom, considering the large quantities of beer he drank. The other prominent symptoms were anorexia and epigastric pain. These will be referred to later.

On examination of the circulatory system, the heart was found to be greatly enlarged (Fig. 1), the maximal cardiac impulse being situated in the fifth space 4 cm. beyond the mid-clavicular line. On auscultation, there was typical presystolic gallop rhythm with a loud apical systolic murmur. The resting pulse rate was 120 and the rhythm regular. The blood pressure was 160/90 mm.; but the diastolic endpoint was poorly defined, the sounds gradually diminishing in intensity and a systolic bruit being heard down to a decompressing pressure of 30 mm.

The knee-jerks could be elicited only on reinforcement and the ankle-jerks were absent. There was no sensory loss to pain, light touch, vibration sense,

or sense of passive movement and position. The urine was acid, with a specific gravity of 1010 : repeated tests failed to show any albumin.



FIG. 1.—Teleradiogram, Nov. 18.

Apart from influenza in 1930, with which he was off work for only one week, there was no previous medical history of significance. He had never suffered from rheumatic fever, sore throats, chorea, scarlet fever, diphtheria, or bronchitis.

Diagnosis.—The clinical picture was atypical. The association of gallop rhythm with extensive œdema, the unusual distribution of the œdema, the

rapidity with which it had appeared and the fact that, until recently, the patient had been a perfectly healthy man suggested that heart failure, in this case, was not due to any of the usual causes.

In searching for an aetiological factor, the possibility of a vitamin deficiency occurred to us. Further enquiry into the history revealed the fact that for seventeen years, during which time he had been employed as a navvy, he had taken 7 to 8 pints of beer daily.

Eighteen months prior to admission he had become a bar attendant, and since then had taken between 14 and 18 pints of beer every day. He had gradually lost appetite and for the greater part of this period had never had more than one meal a day, and had often gone a whole week without eating any solid food. For six weeks he had vomited after every meal.

Cases of beri-beri, such as occur in the East, are rarely seen in Britain ; but a similar clinical picture may be produced by chronic alcoholism, which many workers consider to be a potent factor in inducing dietary deficiency. It leads to anorexia and so to a deficient food intake ; and, since beer is deficient in vitamin B₁ (Donovan and Hanke, 1936), the diet becomes deficient in this vitamin content although its caloric value may be adequate, when little other food is taken. Cowgill (1934) has pointed out that one of the first signs of vitamin B₁ deficiency is anorexia, which in turn leads to further diminution in vitamin intake. Thus a vicious circle is set up. Alcohol can supply a high caloric value with a very low vitamin content. This is the ideal combination for the development of beri-beri, for the higher the caloric intake the greater is the requirement of vitamin B₁.

It is interesting to note that the similarity in distribution of the œdema in cases of chronic alcoholism and "beri-beri heart" should have attracted attention before the connecting link between the two conditions was recognized. Writing in 1906, before vitamins had been discovered, Graham Steell referred to the subject in these words :

"Capricious distribution of dropsy is specially apt to occur in cases of the cardiac muscle-failure of beer-drinkers and of the disease known as beri-beri, of both of which diseases, it is curious to note, peripheral neuritis is a clinical feature. . . . Curious special localizations of œdema met with, in cases of the kind, have been the scrotum, and together the upper trunk, upper extremities, and scalp and neck, so that the œdema simulates that resulting from mediastinal tumour."

Laboratory Investigations.—Electrocardiograms (Fig. 2) showed no significant abnormality. On the third day the T wave in lead III was upright, on the fourteenth day it was almost isoelectric, and a month after admission it was inverted. A similar change was noted by Keefer (1930) in two cases, but it is doubtful whether it is of any significance.

The plasma proteins were not estimated during the acute stage, but ten days after admission the albumin : globulin ratio was 5.5 : 2.0, and a subsequent determination about seven weeks later gave the ratio 5.5 : 2.1. On the third day the blood urea was 20 mg. per 100 cc. and the urea clearance test 67 per

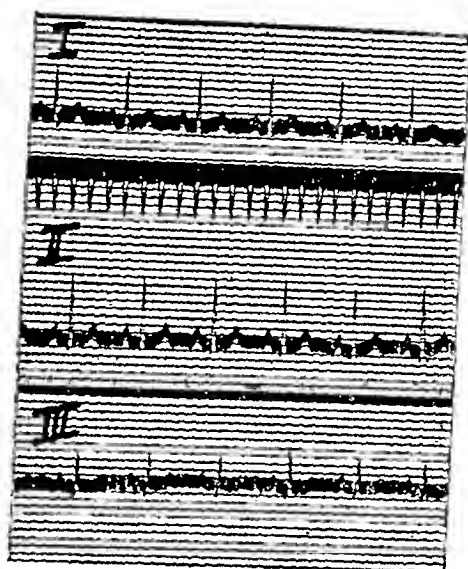


FIG. 2.—Electrocardiogram, Nov. 14. Time intervals, 0.2 sec. Calibration 2 cm.=3mv. A month later T was inverted in lead III.

cent. of the average normal value. A fractional gastric analysis on the fourth day gave a normal result. A blood count on the third day showed :

Red blood corpuscles	4,960,000 per c.mm.
Hæmoglobin	96 per cent.
Colour index	0.97
White blood corpuscles	4,200 per c.mm.

Polymorphs	53.5 per cent.
Lymphocytes	35.5 per cent.
Large mononuclears	7.0 per cent.
Eosinophils	3.5 per cent.
Basophils	0.5 per cent.

A subsequent count, about seven weeks later, showed slightly higher figures for the red cells and hæmoglobin and the white cells had risen to 6000 with 57 per cent. polymorphonuclears, 35 per cent. lymphocytes, and 3 per cent. eosinophils.

Treatment.—The patient was kept in bed and given daily intramuscular injections of 2 mg. of vitamin B₁, in the form of Benerva (Roche) ; the total quantity given during the seventeen days he was in hospital being 30 mg. Apart from a full diet and Easton's syrup, he received no other treatment.

Progress.—For one day the patient refused all food, but then regained his appetite and ate well. During the first day he passed only 16 ounces of urine ; but about twenty-four hours after the first injection of vitamin B₁, a brisk diuresis set in, and in the next three days he passed 196 ounces. His weight on admission was 155 lb. ; four days later it was 146 lb.—a loss of 9 lb. On

admission his pulse rate was 120 ; on the third day it varied between 80 and 90, and a week later had reached a fairly steady level of 60 to 70. These values are recorded graphically in Fig. 3. On the fourth day he felt perfectly

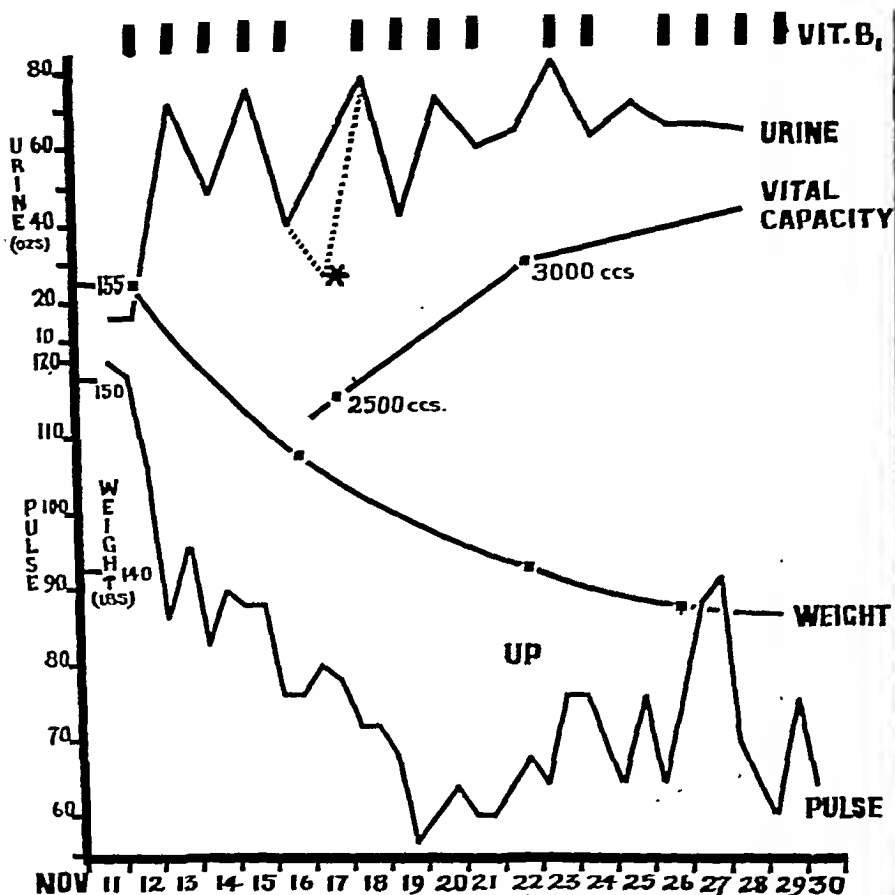


FIG. 3.—Pulse rate, weight, vital capacity, output of urine and dosage of vitamin B₁. Each mark at the top of the figure indicates a dose of 2 mg. vitamin B₁ given intramuscularly. * The whole of the urine was not measured on this date. The vital capacity curve is extrapolated towards a reading taken shortly after the patient was discharged from hospital.

fit, his appetite was excellent, gallop rhythm was no longer present and the oedema had practically disappeared.

The vital capacity on the third day was 2500 c.c. (calculated normal 4175 c.c.) ; five days later it had risen to 3000 c.c. and three weeks after admission it was 3250 c.c. A teleradiogram taken three days after admission showed great cardiac enlargement and considerable pulmonary congestion. Four days later the appearances had altered very little (Fig. 1), but during the next ten days the heart diminished considerably in size (Fig. 4) and the pulmonary congestion completely disappeared.

Ten days after admission he was allowed up and seven days later he was discharged from hospital, since when he has remained fit.



FIG. 4.—Teleradiogram, Nov. 29.

THE BERI-BERI HEART

The classical features of "beri-beri heart" as seen in Java were fully described by Aalsmeer and Wenckebach (1928) and later by Wenckebach (1932 and 1934). These workers emphasized the predominant element of right-sided heart failure without pulmonary congestion. Weiss and Wilkins (1936 and 1937*a*) published a series of 120 cases observed in America, many of which appeared to be attributable to chronic alcoholism. They recorded a large and varied list of signs and symptoms, and stated that the cardiovascular disturbances caused by nutritional deficiency did not form a single rigid clinical syndrome. They

pointed out the importance of dietary deficiency in precipitating cardiac failure in other forms of organic heart disease.

Hawes (1938) described the clinical picture of "shoshin" (the severe form of acute congestive failure due to beri-beri which is seen in the East) as that of a desperately ill patient, vomiting, breathless and restless, with severe epigastric pain, enlarged heart, dependent œdema, engorged veins, tachycardia, and a low diastolic pressure. This description is almost identical with that given by Aalsmeer and Wenckebach (1928) for what they called the "acute pernicious" beri-beri heart. They divided cardiovascular beri-beri into three groups—a mild ambulatory type with dyspnoea and palpitation; a moderately severe type with cardiac enlargement, œdema and polyneuritis; and the acute pernicious form described above.

Our case differs from the moderately severe type by the absence of polyneuritis, yet did not present so advanced a clinical picture as the acute pernicious type. It is very similar to the case described by Price (1938) and to one of those reported in detail by Weiss and Wilkins (1936), both of which were attributed to chronic alcoholism.

The absence of signs of polyneuritis is not uncommon in the more severe and acute forms of beri-beri heart, and Keefer (1930), who described 15 cases of beri-beri heart in Japan, showed that the patients who developed cardiac insufficiency were those with least involvement of the nervous system. He regarded this as due to the protection of the heart by the motor disability caused by the polyneuritis. If this hypothesis be correct, we should not expect to find severe signs of polyneuritis in the more acute forms of beri-beri heart, though Strauss (1938) believes that it is rare to find beri-beri heart without at least minimal signs of polyneuritis. Aalsmeer and Wenckebach (1928), on the other hand, think that cardiac enlargement may be detected long before the appearance of the first signs of polyneuritis. Birch and Harris (1934) state that the biochemical lesion caused by vitamin B₁ deficiency seems to affect the heart almost immediately and may cause sudden death from heart failure, while its toxic action on the central nervous system proceeds more slowly.

ALLIED CONDITIONS

The biochemical mechanism underlying the production of alcoholic beri-beri heart is the subject of controversy, and, although deficiency of vitamin B₁ is of paramount importance, it is possible that this is not the only factor. Before concluding that œdema associated with dietary deficiency is due to lack of vitamin B, other abnormalities in the diet, such as deficiency of proteins or total calories, must be considered, especially when these deficiencies are associated with an increased fluid intake. Such types of deficiency, however, cannot explain the cardiovascular signs and symptoms which are seen in cases like that which we have described, while the plasma protein values reported by Weiss and Wilkins (1936 and 1937*a*), in cases of alcoholic beri-beri are not sufficiently low to account even for the œdema.

The history in our case naturally led us to speculate on the possible relation

of alcoholic beri-beri heart to the so-called beer-drinker's heart. This diagnosis is now rarely made ; in fact, the disease seems almost to have died out. This might be accounted for either by the reduced consumption of beer at the present day, or by the fact that beer-drinker's heart is nothing more nor less than hypertensive heart disease. This latter hypothesis receives support from the fact, pointed out by Weiss and Wilkins (1937*b*), that the disappearance of this disease is chronologically related to the introduction of sphygmomanometry and to the recognition of the importance of hypertension in the production of cardiac hypertrophy and heart failure.

Other forms of œdema associated with dietary deficiency are so-called famine œdema and war œdema. In recent years these conditions have been studied comparatively little ; but most workers believe that they are essentially different from beri-beri. Nixon (1920) regards polyuria, bradycardia and asthenia as the essential clinical features of famine œdema ; whereas the dyspnœa, tachycardia, cardiac dilatation and signs of heart failure found in association with vitamin B₁ deficiency are absent. In fact, the only clinical feature common to the two conditions is the œdema.

The nature of the dietary deficiency in these conditions has been studied by several workers. Maver (1920) has surveyed the whole field and gives a comprehensive bibliography. She does not believe that war œdema is due to a deficiency of one or more specific vitamins, but that it is the result of a protracted existence on a diet deficient in total calories and especially in protein, and that a high fluid intake and possibly a high salt intake are important accessory factors. She points out that a combination of low calories, low protein and excessive fluid intake will lead experimentally to a severe dropsy corresponding in all respects to war œdema. Cowgill (1934) failed to find any evidence of vitamin B₁ deficiency in diets under conditions where such œdema might be expected to occur.

The post-mortem appearances were studied by Porter in the Indian famine of 1877-78 (quoted by Nixon, 1920) and are those of starvation. He demonstrated the changes of brown atrophy in the heart ; this is unlike the post-mortem findings of Aalsmeer and Wenckebach (1928), and Weiss and Wilkins (1936 and 1937*a*) in beri-beri heart. These workers found hydropic degeneration and interstitial œdema of the cardiac muscle.

Thus it appears that these forms of œdema are ætiologically, clinically and pathologically distinct from the œdema associated with beri-beri heart.

DIAGNOSIS OF THE BERI-BERI HEART

Severe cases of beri-beri heart are rare in this country ; yet their recognition is of importance, for they respond dramatically to specific treatment and very poorly to other measures.

The diagnosis rests essentially upon :

1. The dissimilarity of the clinical syndrome from that of heart failure due to other causes.

2. The absence of the more common ætiological factors responsible for producing heart failure.
 3. The presence of a dietary abnormality compatible with a gross deficiency of vitamin B₁.
 4. The response to treatment with vitamin B₁.
- The diagnosis is corroborated by :
5. The presence of other signs and symptoms of vitamin deficiency.
 6. Certain laboratory tests.

1. *The Clinical Syndrome*.—The distribution of the œdema is unusual. It may be most striking in the face and genitalia, and most pronounced in the morning, suggesting renal rather than cardiac insufficiency ; but the absence of albuminuria, the relatively high renal efficiency and the normal protein content of the plasma exclude this diagnosis. In our case there was less venous engorgement than one would expect in view of the extent of the œdema.

The association of gallop rhythm with extensive œdema is unusual in the other types of heart failure, but common in alcoholic beri-beri heart. Weiss and Wilkins (1936) discussed the clinical differences between beri-beri heart as seen in the East and in America, where it is usually due to chronic alcoholism. They emphasized the frequency of combined right and left heart failure in alcoholic beri-beri, whereas in the East right-sided failure is the rule (Aalsmeer and Wenckebach, 1928 ; Wenckebach, 1928) and pulmonary congestion is stated to occur only as a terminal condition (Wenckebach, 1928). In our case the combination of œdema and systemic congestion with gallop rhythm and pulmonary congestion showed that both right and left ventricles had failed.

2. *Ætiology*.—The absence of the more common causes of heart failure first drew attention to our case, and is probably one of the most valuable clinical pointers to the ætiology. There was no evidence of syphilitic, hypertensive or rheumatic heart disease or of heart failure secondary to pulmonary disease.

Other possible causes of œdema must be considered. In beri-beri heart the plasma proteins are sometimes lowered (Weiss and Wilkins, 1936) ; but usually not to such a level as would account for the œdema. In our case they were normal on the tenth day, and before the weight had reached a steady level. Severe anæmia is unusual in beri-beri heart, although common in other forms of œdema associated with dietary deficiency.

(3) *Diet*.—In our case, inquiry into the diet revealed a gross abnormality which left no doubt that a vitamin deficiency must have existed for a considerable time. To justify the assumption of a vitamin deficiency it is essential to establish a gross abnormality of this type. In this country chronic alcoholism is the most frequent cause of such a deficiency, and amongst the reported cases attributed to alcoholism are those of Jolliffe and Goodhart (1938), Price (1938) and many of those recorded by Weiss and Wilkins (1936 and 1937a).

(4) *Vitamin Therapy*.—The therapeutic test is the most convincing diagnostic evidence. Aalsmeer and Wenckebach (1928) thought the effect of vitamin B₁ to be as specific for beri-beri heart as thyroid extract is for myxœdema. Its

action is certainly no less dramatic. In our case, twenty-four hours after the first injection the pulse rate fell, the patient regained his appetite and a brisk diuresis set in.

Rapid response to treatment with vitamin B₁ has been recorded by Weiss and Wilkins (1936), Hashimoto (1937), Strauss (1938) and others. Weiss and Wilkins (1937*b*) state that, in general, the improvement is most rapid in patients with a severe degree of congestive failure of relatively short duration. Nylin (1937) recorded a case which responded very well to intravenous vitamin B₁, although complicated by bilateral pulmonary tuberculosis.

It is important to exclude the possibility that other forms of œdema or heart failure might respond to vitamin B₁ therapy. Weiss and Wilkins (1936) gave doses of 5, 10 and 20 mg. of crystalline vitamin B₁ subcutaneously, intramuscularly, and intravenously to two patients with normal cardiovascular systems, and to three with organic heart disease. They found no significant alternations in heart rate, electrocardiograms, arterial pressure, velocity of blood flow, plasma proteins or in the degree of œdema.

(5) *Other Signs of Vitamin Deficiency.*—These help to corroborate the diagnosis; for instance, the presence of polyneuritis and heart failure, in an alcoholic subject, suggests the possibility of alcoholic beri-beri. The commonest associated lesions are polyneuritis and gastro-intestinal disturbances, particularly anorexia, epigastric pain, and vomiting. It is not unusual to find achlorhydria in beri-beri heart, as in the case recorded by Price (1938). Other common associated lesions mentioned by Weiss and Wilkins (1936) are pellagra-like dermatitis and glossitis.

(6) *Special Tests.*—(a) The estimation of vitamin B₁ in the blood.—This assay has only recently been possible, and, so far as we know, has never yet been made in a case of beri-beri heart; but there is little doubt that it will prove to be of value in these cases when there is better agreement as to the lower limit of the normal range. Wilkinson and Rowlands (1938) regard the threshold as about 6.5 µg per 100 c.c. using the effect of the vitamin on the growth of *Phycomyces blakesleeanus* (Schopfer's method) as the method of estimation.

(b) *The peripheral circulation rate.*—Weiss and Wilkins (1937*b*) state that the combined presence of congestive failure and a relatively or absolutely increased circulation rate is the most outstanding feature of beri-beri heart failure. It would seem, therefore, that the measurement of the peripheral circulation time is an investigation of value when this ætiology is suspected in a case of acute heart failure.

(c) *Aalsmeer's Adrenalin Test.*—This is regarded by many as a valuable diagnostic aid. It depends upon the rapid fall of diastolic pressure and the exacerbation of symptoms which follow the injection of adrenalin. Weiss and Wilkins (1936) record a case which demonstrates how this effect is striking in the acute stages and less so as the clinical condition improves.

(d) *Electrocardiographic changes in the beri-beri heart* have been described by many workers (Aalsmeer and Wenckebach, 1928; Scott and Hermann, 1928; Keefer, 1930; Hashimoto, 1937; Price, 1938; Wenckebach, 1928; Weiss and Wilkins, 1936; Strauss, 1938; and others); but these changes are

often absent, even in cases with advanced heart failure (Aalsmeer and Wenckebach, 1928), and, although the changes are reversible by treatment, they vary widely in character. The only feature of diagnostic value appears to be the shortening of the P-R interval described in a few cases by Aalsmeer and Wenckebach (1928) and by Price (1938). Chopra, Choudhuri, and De (1937) noted similar changes in 40 per cent. of cases of epidemic dropsy in India. It is only where the electrocardiogram shows changes reversible by vitamin B₁ therapy that it can be accepted as affording evidence of value in diagnosis. In our case, the electrocardiogram was within normal limits throughout, but the T wave in lead III, which was upright during the acute stage (Fig. 2), became inverted a month later. This was also noted in two cases by Keefer (1930), but we do not attach any significance to this finding.

LESSER DEGREES OF VITAMIN B₁ DEFICIENCY

If gross deficiency of vitamin B₁ can produce such striking cardiovascular disturbances, it seems probable that less severe deficiency, which must be much more common, often passes unrecognized, and may contribute to the development of cardiac failure in patients with rheumatic, syphilitic, or hypertensive heart disease. It is, therefore, important to inquire into the diet of patients with these forms of heart disease, especially when cardiac failure occurs without adequate cause.

Weiss and Wilkins (1937a) state that cardiovascular disturbances attributable to deficiency of vitamin B₁ occurred in 35 out of 5506 admissions to the Boston General Hospital medical wards during two years. They regard this form of cardiovascular disease as more frequent than congenital heart disease, adhesive pericarditis, hyper- or hypothyroid heart disease and subacute bacterial endocarditis. It is probable that some cases of beri-beri heart escape recognition, and that the heart failure is attributed to other causes.

SUMMARY

A bar attendant, aged 36, with a history of chronic alcoholism and gross dietary deficiency, with anorexia, vomiting, epigastric pain, extensive œdema, a greatly enlarged heart, gallop rhythm and tachycardia, was treated with parenteral vitamin B₁. He lost his œdema and other signs of cardiac failure in five days, the heart diminished greatly in size, and he was discharged cured seventeen days after admission.

The case is compared with others that have been reported and the diagnosis of the condition is discussed.

We are indebted to our colleague Dr. E. W. Twining for the two radiograms.

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THE DRUG TREATMENT OF HYPERPIESIA

BY

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The more numerous the remedies for a disease the less likely that any will prove consistently helpful. Of the many drugs recommended for hyperpiesia (essential hypertension) there is no agreement on the best to employ, and none has gained any outstanding reputation. There seems to be no authoritative statement on the comparative value of these remedies, and individual drugs have been praised without controlled clinical observations. The urge for trying new remedies in hyperpiesia is prompted by the common incidence of a condition which produces bizarre symptoms and determines many complications. Although for this reason treatment is a matter of great concern, it is not likely to be very successful while the cause remains unknown.

This paper deals primarily with the effects of certain drugs on the blood pressure in patients with hyperpiesia, and also records our observations on the influence of changes in the blood pressure on the subjective symptoms. We are not concerned here with the advisability of reducing blood pressure in hyperpiesia, but our findings during short periods of a lowered pressure have convinced us that the presence of symptoms has little or no relation to the level of the blood pressure. The opportunity, however, of observing the results of a greatly lowered blood pressure in hyperpiesia over a long period has only been gained through the onset of cardiac infarction or heart failure, when the appearance of newer symptoms might mask the direct effects of the lowered pressure.

METHOD OF OBSERVATION

We submitted the following preparations to clinical trial: sodium nitrite, glyceryl trinitrate, erythrol tetranitrate, mannitol hexanitrate, bismuth subnitrate, potassium iodide, iodine, potassium bromide, sodium luminal, chloral hydrate, papaverine sulphate, euphyllin, diuretin, theominal, doryl, pacyl, hypotan, calcium chloride, atropine, potassium thiocyanate, benzyl benzoate, guipsine, detensyl, phyllosan, citrin, yohimbine hydrochloride, padutin, vagotonine, angioxyl, bioglan H, anabolin, perandren, and œstrone. We selected these remedies either on account of a reputation which they already held in the treatment of hyperpiesia or on account of their pharmacological action in producing a fall in blood pressure. Many of the proprietary preparations were

enlisted for trial not with any faith in their reputed hypotensive qualities but for the purpose of comparing their effects with those of the active drugs. In this way we added to our controls.

The preparations were tried in 70 patients, 13 of whom were males and 57 females. The ages varied from 38 to 72 years and the average age was 58. Before admission into the series each patient was judged to be a case of hypertension after a routine clinical examination which included urine analysis, tests of renal function, retinoscopy, electrocardiography, and radiocardiography. On radiocardiography, left ventricular enlargement and distortion of the aorta in the form of an unfolding were sought, and when either change preponderated it was noted. Any patient whose systolic blood pressure was less than 160 mm. Hg or whose diastolic blood pressure was less than 100 mm. was excluded from the series. Again, patients in whom a blood pressure of 160/100 was recorded at the first examination were not admitted unless they showed a rise above this at one of two other observations. Any patient with a systolic pressure of 200 mm. or over was not excluded simply because the diastolic pressure was less than 100 mm. No patient with evidence of nephritis was admitted. Any who failed to co-operate during the course of the investigation was rejected.

Each patient attended the London Hospital at fortnightly intervals, but whenever a drug required parenteral administration or closer observation of its effects he was admitted into hospital. At each attendance a resting period of half an hour or longer was assured before starting observations. Questions were then asked about progress during the trial period, any change in symptoms, the occurrence of untoward or toxic manifestations, and any variation in the patient's activity or habits which might influence the course of progress. The blood pressure was then taken (to the nearest multiple of 5 mm.) under conditions which were constant and standard for each patient. The investigation lasted for eighteen months, and over a thousand blood pressure readings were recorded, representing a similar number of observation periods each of a fortnight's duration. We came to place greater reliance on frequent controlled readings of the blood pressure in a limited number of co-operative patients, and so avoided retaining too many in the series.

The drugs were always given in adequate and usually in optimum doses, and this ensured that each patient was under the full influence of the drug soon after the start of the trial period. Although the *daily* dosage is instanced under each drug, it is to be understood that this was dispensed as three separate doses during the day. If symptoms of intolerance appeared it was discontinued, but was often given another trial after a suitable lapse of time. Although a single trial period usually permitted an opinion on the efficiency of a drug in reducing the blood pressure value, it was as a rule tried over several consecutive periods in a certain number of patients.

Before a remedy was judged to have established a claim to be of value as a hypotensive agent, it had to satisfy certain standards of efficiency. First, it had to be capable of reducing the blood pressure when this was raised and of maintaining it at the lower value. Secondly, it had to demonstrate this action

consistently and in a high proportion of patients, thus proving an effect distinct from the lowered pressure which occurs as a natural periodic variation in a patient with hyperpiesia without treatment. Thirdly, this reduction had to be obtained without any toxic-symptoms.

It therefore became necessary to know the extent to which the blood pressure fluctuated naturally apart from the influence of any active drug. In a series of 650 school children of the ages of 10 to 17 years Lord Dawson (1925) found among 52 in whom the systolic pressure exceeded 130 mm. that this higher reading only remained consistently high in 17 per cent., while in the remaining 83 per cent. it was inconstant. To gain a knowledge of this natural variation in our patients we made use of frequent test periods when the patient was taking a simple placebo mixture, interspersed among test periods allotted to active drugs. The result of one such observation is charted in Fig. 1. Again, many

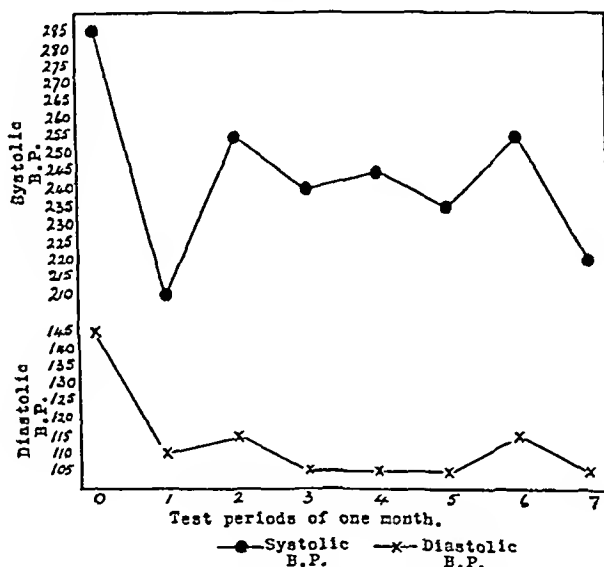


FIG. 1.—Blood pressure in a female, aged 58, with hyperpiesia, during a period of seven months when a placebo mixture was the only treatment given.

patients with hyperpiesia were observed throughout when taking only placebo mixtures, while some of those with obesity were observed during dietetic treatment and without medicine. In this way we feel that our evaluation of drugs used in the treatment of hyperpiesia, based as it is on strictly controlled observations, is substantially accurate. The second part of Fig. 2 illustrates the scheme of our observations during successive test periods of 14 days on the different drugs; the first part showing the effect of a reducing diet (see later).

RESULTS

If the blood pressure did not rise or fall at the end of a test period by more than 10 mm., we regarded it as showing no change. If the blood pressure fell

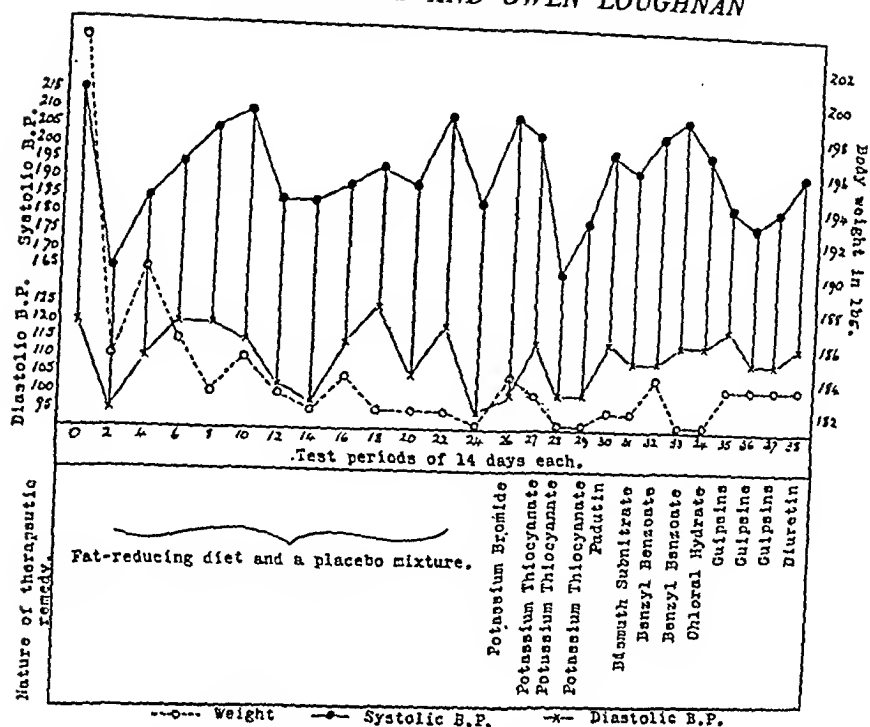


FIG. 2.—Blood pressure in a male, aged 57, with hyperpiesia, during treatment with a fat-reducing diet and later with certain active drugs.

by 10 mm. during successive observation periods, when statistically it would continue to be regarded as showing no change, we recorded it as showing a fall in the second instance. If a rise or fall of 11 to 25 mm. occurred, we have classified it as a moderate; and if of 26 mm. or over, as a conspicuous change. These figures apply to the systolic pressure, because we found that it was the more dependable figure upon which to judge the variation. The diastolic figure usually showed the same kind of change as the systolic, but not to the same extent, while its exact estimation could not be determined as readily as the systolic. If perchance a prominent change in the diastolic value was not also shown in the systolic value, we were careful to record it.

NITRITES

The effects of sodium nitrite on the blood pressure in healthy subjects and in patients with hyperpiesia were observed by Weiss and Ellis (1933); a fall usually occurred within 5 to 15 minutes after 1 to 5 grains had been taken by mouth, and averaged 12 mm. for 30 minutes in the healthy subjects and 35 mm. for two hours in the patients with hypertension.

A transient fall in the blood pressure follows the administration of amyl nitrite. Zeiss and Brams (1930) observed the action of amyl nitrite and glyceryl trinitrate on the blood pressure in 10 patients with hyperpiesia and in 10 healthy subjects. Amyl nitrite produced a fall in each of these cases, and glyceryl

trinitrate (1/50 grain by mouth) reduced it temporarily in the healthy subjects but not always in the patients with hyperpiesia. The effects of the two drugs were also noted by Burgess (1931); amyl nitrite reduced the blood pressure in both groups, but glyceryl trinitrate, in doses of 1/100 to 1/50 grain by mouth or 1/200 grain subcutaneously, did not produce a constant effect.

In successive papers Stieglitz (1927, 1928, 1930, and 1932) has extolled the value of bismuth subnitrate as a vasodilator and as a hypotensive agent in patients with hyperpiesia. He postulated that the beneficial effect depended on the gradual vasodilatation resulting from the continuous absorption of small quantities of nitrite ions and a reduction of the blood chloride which follows the diuretic action of the nitrate ion. Ayman (1932) tried bismuth subnitrate in daily doses of 30 grains for periods of three to nine months in 15 patients with hyperpiesia; his observations were carefully controlled and he concluded that the drug had not lowered the blood pressure in a single case. Bruen (1932) observed the hypotensive action of bismuth subnitrate in healthy subjects, and in 1934 was able to report on such a trial in a series of patients with hyperpiesia. The observations were carefully controlled, so that periods on lactose tablets and oxalate powders were compared with periods on 30, 60, and 90 grains of bismuth subnitrate daily. He concluded that bismuth subnitrate was without influence on either the blood pressure or the symptoms.

Amyl Nitrite.—We observed the effect on the blood pressure of inhalation of amyl nitrite (5 minims) in 22 patients with hyperpiesia and in 18 healthy subjects. There was a fall in both systolic and diastolic pressure in each of the 40 cases, but the change was more noticeable in the former. In the patients with hyperpiesia the systolic fall varied from 10 to 100 mm., and averaged 45 mm. The average time before the fall took place was one minute and its average duration was three minutes. A compensatory rise of an average of 22 mm. only followed in four instances (Fig. 7). In the healthy subjects the systolic fall varied from 10 to 60 mm. and averaged 33 mm. The average time before the fall took place was one minute and its average duration was six minutes. A compensatory rise of an average of 36 mm. followed in four instances.

Glyceryl Trinitrate.—We also observed the effects on the blood pressure when this was *chewed* in tablets containing 1/100, 1/50, 1/25, and 1/12 grain, in 7 patients with hyperpiesia and in 5 healthy subjects. A fall in both systolic and diastolic pressure occurred in each of the 12 cases. The systolic fall was the more noticeable, and in the hypertensive group varied from 25 to 195 mm. with an average of 55 mm. The average time before the fall took place was 6 minutes and its average duration was 16 minutes. In the healthy subjects the fall varied from 15 to 40 mm. with an average of 26 mm. The average time before the fall took place was 4 minutes and its average duration 16 minutes. A compensatory rise of the blood pressure value was not seen in either group.

Inhalation of amyl nitrite and the chewing of glyceryl trinitrate will therefore always cause the systolic blood pressure to fall, both in normals and in patients with hyperpiesia, the extent of the fall being greater in the latter. The fall produced with glyceryl trinitrate appears later than with amyl nitrite, but the effect lasts longer. The transient changes indicate that amyl nitrite and glyceryl

trinitrate are unlikely to prove of value in the continuous treatment of hyperpiesia.

Sodium nitrite was submitted to a controlled clinical trial in 19 patients with hyperpiesia, and its effect observed in a daily dosage of 15 grains (0.9 g.) during 22 test periods.* A moderate fall occurred during 2 test periods, but it did not persist when the drug was continued. There was no change during 6, and a moderate rise took place during 6 test periods; in 8 the effect could not be recorded as the patients failed to continue taking the drug.

Symptomatic improvement was recorded during 3 test periods on sodium nitrite, but during 19 the symptoms either remained stationary or became aggravated. Toxic effects, namely giddiness, palpitation, headache, and weakness occurred in 13, and in 8 the symptoms compelled the patients to discontinue its use.

Glyceryl trinitrate was tried in 11 patients with hyperpiesia, and its effect observed in a daily dosage of $1/33$ grain (0.0018 g.) given by mouth during 11 test periods. A fall occurred during 2 test periods, conspicuous in one and moderate in the other. There was no change during 1, and a rise took place during 4, conspicuous in 1 and moderate in 3. The effects could not be recorded in 4 instances as the patients failed to take the tablets because of faintness, giddiness or palpitation.

Symptomatic improvement was recorded during 1 test period on glyceryl trinitrate, but during 10 the symptoms either remained stationary or became aggravated.

Erythrol tetranitrate was tried in 13 patients with hyperpiesia, and its effect observed in a daily dosage of $1\frac{1}{2}$ grains (0.09 g.) during 19 test periods. A fall occurred during 7, conspicuous in 5 and moderate in 2; there was no change during 6; and a rise took place during 6, conspicuous in 1 and moderate in 5.

Symptomatic improvement was recorded during 6 test periods on erythrol tetranitrate, but during 13 the symptoms either remained stationary or became aggravated. Toxic effects, namely giddiness and headache, occurred twice.

Mannitol hexanitrate was tried in 24 patients with hyperpiesia, and its effect observed in a daily dosage of 6 grains (0.36 g.) during 29 test periods. A fall occurred during 8, conspicuous in 4 and moderate in 4; there was no change during 5; and a rise took place during 9, conspicuous in 1 and moderate in 8. In 7 it was not possible to record its effects because the patients failed to continue taking the drug on account of dizziness and headache.

Symptomatic improvement was recorded during 6 test periods on mannitol hexanitrate, but during 23 the symptoms either remained stationary or became aggravated.

Bismuth subnitrate was tried in 22 patients with hyperpiesia, and its effect observed in a daily dosage of 60 grains (3.6 g.) during 39 test periods. A fall occurred during 8, conspicuous in 3 and moderate in 5; there was no change during 17; and a rise took place during 14, conspicuous in 5 and moderate in 9.

Symptomatic improvement was recorded during 24 test periods on bismuth

* A test period means in each case a period of 14 days.

subnitrate, but during 15 the symptoms either remained stationary or became aggravated. Toxic effects were not seen.

A comparison of these results with those obtained from placebo treatment is made in Table I.

TABLE I

COMPARING THE EFFECTS OF NITRITES AND PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure Value			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Sodium nitrite ..	22 (60)	14 (30)	43 (57)	43 (13)	14 (33)	86 (67)
Glyceryl trinitrate ..	11 (27)	28 (37)	15 (48)	57 (15)	10 (40)	90 (60)
Erythrol tetranitrate	19 (38)	36 (42)	32 (39)	32 (19)	32 (37)	68 (63)
Mannitol hexanitrate	29 (59)	36 (34)	23 (55)	41 (11)	20 (36)	80 (64)
Bismuth subnitrate	39 (40)	20 (30)	44 (65)	36 (5)	61 (33)	39 (67)

Figures, excepting those in the first column, denote percentage of test periods: Figures in brackets apply to the placebo mixture.

IODINE

Potassium iodide intravenously often causes the blood pressure to fall, but Macht (1914) showed that its hypotensive effect was due to potassium and not the iodine ion. Mosenthal (1933) obtained hypotensive effects from the use of sodium and potassium iodide in daily doses of 3 to 10 grains in cases of hypertension. The use of iodine in hyperpiesia is also mentioned by others (Norris, Bazett, and McMillan, 1927 ; Gager, 1930 ; Hay, 1931 ; Parkinson, 1936 ; White, 1937). Livingstone (1935) advocated the use of Lugol's iodine. Lewis (1937), speaking on drugs used in hyperpiesia, said that none offered much prospect of benefit and that even potassium iodide, which had long been favoured as a remedy, was losing its reputation in this field.

Iodine, as Lugol's solution, was tried in 20 patients with hyperpiesia, and its effect observed in a daily dosage of 18 minims (1.1 c.c.) during 42 test periods. A moderate fall occurred during 5 test periods ; there was no change during 28 ; and a rise during 9, conspicuous once and moderate in 8.

Symptomatic improvement was recorded during 18 test periods on iodine, but during 24 the symptoms either remained stationary or became aggravated.

Potassium iodide was submitted to a controlled clinical trial in 23 patients with hyperpiesia, and its effect observed in a daily dosage of 30 grains (1.8 g.) during 28 test periods. A fall occurred during 4 test periods, conspicuous in 1 and moderate in 3 ; there was no change during 19 ; and a rise took place during 5, conspicuous in 4 and moderate once.

Symptomatic improvement was recorded during 10 test periods on potassium iodide, but during 18 the symptoms either remained stationary or became aggravated.

A comparison of these results with those obtained from placebo treatment is made in Table II.

TABLE II
COMPARING THE EFFECTS OF IODINE AND PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure Value			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Iodine	42 (53)	10 (26)	67 (57)	23 (17)	43 (30)	57 (70)
Potassium iodide ..	28 (53)	14 (29)	68 (48)	18 (23)	36 (30)	64 (70)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

SEDATIVES

Bromide.—We have not found reports of any observations on the effects of bromide on the blood pressure in hyperpiesia, but its use has been mentioned especially in connection with the relief of symptoms (Gager, 1930 ; Hay, 1931 ; Parkinson, 1936 ; White, 1937).

Potassium bromide was tried in 40 patients with hyperpiesia, and its effect observed in a daily dosage of 30 grains (1·8 g.) during 66 test periods. A fall occurred during 21, conspicuous in 8 and moderate in 13 ; there was no change during 29 ; and a rise took place during 16, conspicuous in 6 and moderate in 10.

Symptomatic improvement was recorded during 27 test periods on potassium bromide, but during 39 the symptoms either remained stationary or became aggravated.

Sodium Luminal.—Gruber and others (1925) gave luminal in daily doses of $4\frac{1}{2}$ grains to 36 patients with hypertension, and found a fall in pressure in 85 per cent., but the degree of this fall is not given, and it was not maintained on prolonged administration. Hay (1931) attributed to luminal a slight hypotensive as well as sedative effect, but this action was evanescent and was more likely to prove beneficial in early cases. Parkinson (1936) favoured luminal along with bromide in relieving symptoms, particularly palpitation and restlessness. Adson and Allen (1937) regarded sedatives, especially the barbiturates, as the most valuable drugs in high blood pressure, and stated that under controlled conditions it fell to normal in many patients, and that the dosage should be adjusted to secure a sedative action without causing drowsiness.

We submitted sodium luminal to trial in 38 patients with hyperpiesia, and observed its effect in a daily dosage of $1\frac{1}{2}$ grains (0·09 g.) during 52 test periods. A fall occurred during 14, conspicuous in 5 and moderate in 9 ; there was no change during 26 ; and a rise took place during 12, conspicuous in 2 and moderate in 10.

Symptomatic improvement was recorded during 21 test periods on sodium luminal, but during 31 the symptoms either remained stationary or became aggravated. Toxic effects were not seen.

Chloral Hydrate.—Matte and Dias-Cavaroni (1926) reported on an investigation of the effects of certain drugs on the blood pressure in cases of hyperpiesia. They found that chloral hydrate frequently reduced the systolic pressure, but that this effect seldom lasted more than ten days.

We submitted chloral hydrate to a trial in 23 patients with hyperpiesia, and observed its effect in a daily dosage of 30 grains (1.8 g.) during 33 test periods. A fall occurred during 10 test periods, conspicuous in 4 and moderate in 6; there was no change during 17; and a rise took place during 5, conspicuous in 2 and moderate in 3. In one instance the effect could not be recorded, because of dizziness and headache.

Symptomatic improvement was recorded during 7 test periods on chloral hydrate, but during 26 the symptoms either remained stationary or became aggravated.

Papaverine Sulphate.—Reporting on an experimental study of papaverine sulphate, Macht (1916) stated that it slowed the heart rate and reduced the blood pressure through vasodilatation of the peripheral arteries. The use of opium was mentioned by Norris, Bazett, and McMillan (1927), and White (1937) mentioned papaverine in the treatment of hyperpiesia, but expressed no opinion as to its value.

We submitted papaverine sulphate to a trial in 16 patients with hyperpiesia, and observed its effect in a daily dosage of $7\frac{1}{2}$ grains (0.45 g.) during 24 test periods. A fall occurred during 8, conspicuous in 4 and moderate in 4; there was no change during 13; and a moderate rise took place during 3.

Symptomatic improvement was recorded during 6 test periods on papaverine sulphate, but during 18 the symptoms either remained stationary or became aggravated. Toxic effects were not seen.

A comparison of these results with those obtained from placebo treatment is made in Table III.

TABLE III

COMPARING THE EFFECTS OF SEDATIVE DRUGS AND PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Potassium bromide	66 (90)	32 (31)	44 (52)	24 (17)	41 (34)	59 (66)
Sodium luminal ..	52 (90)	27 (31)	50 (51)	23 (18)	40 (30)	60 (70)
Chloral hydrate ..	33 (43)	30 (29)	55 (56)	15 (15)	20 (30)	80 (70)
Papaverine sulphate	24 (31)	34 (42)	54 (46)	12 (12)	25 (32)	75 (68)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

XANTHINE DERIVATIVES

The xanthine derivatives have been mentioned in connection with the treatment of hyperpiesia by Livingstone (1935), White (1937), and Lewis (1937), but without an opinion on their actual value as hypotensive agents. Calcium diuretin, in the experience of Basch (1924), caused the blood pressure in hypertension to fall at times as much as 40 mm. and to remain at the lowered figure; and Kaiser (1925) also obtained good results from it.

We submitted *euphyllin* (theophylline-ethylene-diamine) to a trial in 31 patients with hyperpiesia, and observed its effect in a daily dosage of 9 grains (0.6 g.) during 41 test periods. A fall occurred during 11 test periods, conspicuous in 4 and moderate in 7; there was no change during 23; and a rise took place during 7, conspicuous in 2 and moderate in 5.

Symptomatic improvement was recorded during 10 test periods on *euphyllin*, but during 31 the symptoms either remained stationary or became aggravated. Toxic effects, namely weakness, insomnia, headache, and palpitation occurred twice.

We submitted *diuretin* (theobromine-sodio-salicylate) to a trial in 26 patients with hyperpiesia, and observed its effect in a daily dosage of either 30 grains (1.8 g.) or 45 grains (2.7 g.) during 30 test periods. A fall occurred during 5 test periods, conspicuous in 1 and moderate in 4; there was no change during 16; and a rise took place during 4 test periods, conspicuous in 1 and moderate in 3. In 5 instances the effects could not be recorded because the patients failed to continue taking the drug on account of giddiness, headache and sickness. These symptoms were also present in three others and were more noticeable with the larger dose.

Symptomatic improvement was recorded during 4 test periods on *diuretin*, but during 26 the symptoms either remained stationary or became aggravated.

A comparison of the results of these drugs and theominal with those obtained from placebo treatment is made in Table IV.

TABLE IV

COMPARING THE EFFECTS OF DRUGS BELONGING TO THE XANTHINE GROUP AND PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure Value			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
<i>Euphyllin</i>	41 (81)	27 (31)	56 (54)	17 (15)	24 (33)	76 (67)
<i>Diuretin</i>	30 (64)	20 (30)	64 (57)	16 (13)	13 (33)	87 (67)
<i>Theominal</i>	21 (48)	23 (40)	53 (44)	24 (16)	33 (31)	67 (69)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

We submitted *theominal* (sodium luminal and theobromine) to a trial in 16 patients with hyperpiesia, and observed its effect in a daily dosage of 30 grains

(1.8 g.) during 21 test periods. A moderate fall occurred during 4 test periods ; there was no change during 9 ; and a rise took place during 4, conspicuous in one and moderate in 3.

Symptomatic improvement was recorded during 7 test periods on thecominal, but during 14 the symptoms either remained stationary or became aggravated. Toxic effects, namely giddiness or drowsiness, occurred four times, and compelled the patients to discontinue its use.

CHOLINE DERIVATIVES

Acetylcholine.—A fall in blood pressure as a result of vasodilatation was shown in the cat by Dale (1914) after small doses of this intravenously. Wolff (1929) was also able to show vasodilatation in organs supplied by the parasympathetic nervous system and a generalized dilatation of the cutaneous arterioles. Meakins and Scriven (1931) recorded a fall of from 25 to 40 mm. in 72 per cent. of their observations on seven cases of hypertension following intramuscular injections of 0.1 to 0.2 g. of acetylcholine ; the effect lasted from one to four hours. Only three out of thirteen healthy subjects showed an appreciable fall in blood pressure after intravascular administration of 2 per cent. acetylcholine given at the rate of 0.02 to 0.14 g. per minute (Ellis and Weiss, 1932). Carmichael and Fraser (1933) gave it intravenously in doses of from 0.01 to 0.03 g. to 46 subjects, and cardio-inhibitory effects appeared within five to ten seconds, but lasted only a few seconds. The slowing of the heart rate was followed by an acceleration, and the systolic and diastolic pressure fell during the phase of slow heart rate, but returned to normal or even higher during the phase of increased heart rate. More recently Fraser (1938) stated that the administration of acetylcholine in man gave disappointing therapeutic results ; when given intravascularly the effects are too brief, and when given intramuscularly too uncertain.

Doryl (carbaminoyl-choline) and Mecholin (acetyl- β -methyl-choline) are more stable than acetylcholine and are active even when given by mouth. Their hypotensive properties have been demonstrated by Kreitmair (1932), Dautrebande (1933) and Fraser (1938), but Fraser has pointed out that both preparations are valueless in the treatment of hyperpiesia, except for the relief of hypertensive headache. Pacyl is another choline derivative which is said to be active when given by mouth. Lewy (1928) and Ganter (1928) reported hypotensive effects and symptomatic improvement from its use. The preparation hypotan is a mixture of methylacetylcholine, bromocholine bromide and chloral hydrate. Its use in hypertension has been recommended on account of its alleged action as a vasodilator.

We submitted *doryl* to a controlled clinical trial in 11 patients with hyperpiesia, and observed its effect in a daily dosage of 6 tablets during 12 test periods. A temporary moderate fall occurred during 1 test period ; there was no change during 4 ; and a rise took place during 3 test periods, conspicuous in 2 and moderate in 1. The effect could not be recorded in 4 instances because the patients failed to continue taking the preparation.

Symptomatic improvement was recorded during 3 test periods on doryl, but during 9 the symptoms either remained stationary or became aggravated. Toxic effects, namely sweating, weakness, giddiness and nausea, occurred in 5 instances.

Pacyl was tried in 11 patients with hyperpiesia, and its effect on the blood pressure in a daily dosage of 6 tablets observed during 22 test periods. A fall occurred during 4, conspicuous in 2 and moderate in 2; there was no change during 15; and a rise took place during 3, conspicuous in 1 and moderate in 2.

Symptomatic improvement was recorded during 10 test periods on *pacyl*, but during 12 the symptoms either remained stationary or became aggravated.

Hypotan was tried in 19 patients with hyperpiesia, and its effect observed in a daily dosage of 8 tablets during 36 test periods. A fall occurred during 10, conspicuous in 3 and moderate in 7; there was no change during 16; and a rise took place during 10, conspicuous in 5 and moderate in 5.

Symptomatic improvement was recorded during 14 test periods on *hypotan*, but during 22 the symptoms either remained stationary or became aggravated.

A comparison of these results with those obtained from placebo treatment is made in Table V.

TABLE V

COMPARING THE EFFECTS OF ACETYLCHOLINE DERIVATIVES AND PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure Value			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Doryl	12 (34)	12 (41)	50 (53)	38 (6)	25 (47)	75 (53)
Pacyl	22 (22)	18 (32)	68 (63)	14 (5)	46 (45)	54 (55)
Hypotan	36 (39)	27 (38)	45 (54)	28 (8)	39 (38)	61 (62)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

OTHER CHEMICAL DRUGS

Calcium Chloride.—The neutralizing action of calcium and potassium chloride on the pressor substances of the guanidine series was mentioned by Major (1925). Addison and Clark (1925) treated 45 patients with hypertension with calcium chloride in daily doses of 90 to 180 grains, and found a persistent fall of 30 mm. or more in the systolic pressure and of 12 mm. or more in the diastolic pressure in 26 cases. Altnow and O'Hare (1927) used calcium chloride and atropine in the treatment of 11 cases with hypertension; no fall in pressure was noticed in 6 and it was insignificant in the remaining 5 patients.

Calcium chloride was tried in 20 patients with hyperpiesia, and its effect observed in a daily dosage of 90 grains (6 g.) during 25 test periods. A fall

occurred during 4, conspicuous in 1 and moderate in 3 ; there was no change during 11 ; and a rise took place during 6, conspicuous in 2 and moderate in 4. In 4 other instances it was not possible to record the effects because of a burning taste in the mouth, sickness or epigastric pain.

Symptomatic improvement was recorded during 6 test periods on calcium chloride, but during 19 the symptoms either remained stationary or became aggravated.

Atropine.—This has been recommended for hypertension on the assumption that raised blood pressure is the outcome of an unbalanced action in the autonomic system, so that the vagal action preponderates over the sympathetic. Altnow and O'Hare (1927) treated 11 patients with calcium chloride and atropine, but without any change in 6 and with an insignificant change in the remaining 5. Norris, Bazett, and McMillan (1927) stated that experimentally atropine raises the blood pressure through stimulation of the vasoconstrictor centre and raising the pulse rate, but that this pressor effect was rarely met with clinically. White (1937) also mentioned the use of atropine in hypertension.

We submitted atropine sulphate to a trial in 9 patients with hyperpiesia, and observed its effect in a daily oral dosage of 1/20 grain (0.003 g.) during 9 test periods. A moderate fall occurred during 1 test period ; there was no change during 5 ; and a rise took place during 2, conspicuous in 1 and moderate in another. In one instance it was not possible to record the effects because of dryness of the mouth and mistiness of vision, and these symptoms were also present in 6 others who persisted with the drug.

Symptomatic improvement was recorded during 3 test periods on atropine sulphate, but during 6 the symptoms either remained stationary or became aggravated.

Potassium Thiocyanate (potassium rhodanate).—During a clinical trial of the effects of cyanate in patients suffering from neurasthenia, Pauli (1903 and 1904) observed both a reduction in the pressure and an improvement of symptoms when hypertension was present. Nichols (1925) stated that the drug was excreted slowly and that cumulative effects might appear ; it was, however, excreted unchanged without the formation of the poisonous prussic acid radicle. Therapeutically he found it reduced the blood pressure to a greater extent than any other drug in hyperpiesia. Smith and Rudolf (1928) gave sodium sulphocyanate to five healthy subjects and to 72 cases with hypertension, the daily dose for one group being 5 grains, for another 10 grains and for a third 15 grains. A fall in blood pressure occurred in each of the healthy subjects and each of the patients with hypertension, and the change was more noticeable in the latter. They observed a fall of as much as 100 mm. in the systolic pressure, and as a rule the greater fall followed the greater dosage. Better results were obtained in those patients without evidence of renal damage and in those who showed the least amount of arterial changes from atheroma. No severe toxic symptoms were noticed. Gager (1928) observed the effects of smaller doses (4½ grains or less daily) of sulphocyanate in 25 patients with hyperpiesia. It was lowered in 22, sometimes by 20 to 60 mm. The fall in the diastolic pressure was not as conspicuous. Subjective improvement was often recorded. Palmer, Silver,

and White (1929) using the same dosage as Gager in 59 cases of hyperpiesia found a reduction of 30 mm. or more in the systolic pressure in 42 per cent. Fineberg (1930), comparing the effects of thiocyanate and sedatives, found that the blood pressure was more often reduced by thiocyanate, but that greater subjective improvement followed sedatives. During controlled observations in 25 patients, Egloff, Hoyt, and O'Hare (1931) obtained a favourable response twice only. Treatment of 99 patients with hypertension with sulphocyanate in doses varying from 5 to 15 grains daily over periods up to three years resulted in a reduction of blood pressure in 68 per cent. (Bolotin, 1932). Both Palmer (1932) and Goldring and Chassis (1932) found that thiocyanate reduced the pressure in 31 per cent. of cases; but Palmer found it did not persist and that often where it had fallen initially with treatment a retrial failed to reproduce this effect. Goldring and Chassis found toxic symptoms in 17 per cent. of their cases, and two deaths were attributed to the drug. A fall in the pressure was noted by Ayman (1931) in 20 of 31 cases with hyperpiesia, but in 19 out of the 20 it was accompanied by distressing toxic symptoms, both in large doses over short periods and in small doses over longer periods. Barker (1936 and 1937) stressed the importance of estimating the cyanate content of the blood during treatment, and thought the optimum benefit occurred when it was maintained at 8 to 12 mg. per 100 c.c.; when it reached 15 to 30 mg. toxic symptoms appeared. The standard concentration in the blood was never obtained by a constant cyanate dosage. He stated that if the concentration was maintained at a suitable level, a fall in blood pressure and symptomatic improvement would be expected in 50 per cent. of cases. When this standard concentration was maintained in 16 patients with hypertension, Griffith and Lindauer (1937) found that both the systolic and diastolic blood pressure became lowered in 10 with improvement of general symptoms and without any severe toxic effects. Massie, Ethridge, and O'Hare (1938) gave sodium thiocyanate to 14 patients with hyperpiesia, under controlled conditions, and found it reduced the pressure and improved the symptoms.

We submitted potassium thiocyanate to a trial in 38 patients with hyperpiesia, and observed its effect in a daily dosage of $4\frac{1}{2}$ grains (0.3 g.) during 90 test periods. A fall occurred during 34, conspicuous in 11 and moderate in 23; there was no change during 36; and a rise took place during 20, conspicuous in 6 and moderate in 14.

Symptomatic improvement was recorded during 31 test periods on potassium thiocyanate, but during 59 the symptoms either remained stationary or became aggravated. Toxic effects were not seen.

Benzyl Benzoate.—Macht (1918), as the result of experiments in animals, found this diminished the tonicity of smooth muscle, and decided on a clinical trial in intestinal colic, bronchial spasm and angiospasm. Using 45 minims of a 20 per cent. alcoholic solution daily he claimed good results in 100 cases, including many with hyperpiesia. Later Macht (1920) reaffirmed his opinion on its beneficial effects and gave further examples in which a raised blood pressure had been reduced by the daily administration of from 60 to 90 minims of the 20 per cent. alcoholic solution. These observations were not con-

trolled and the proportion responding successfully was not expressed. Laubry and Mougeot (1921) submitted benzyl benzoate to a clinical trial and concluded that it was a useful drug to combine with others because it gave results which were sometimes surprising, rarely negligible, and never harmful. Gruber and Shackelford (1924) gave 120 minims of the 20 per cent. alcoholic solution of benzyl benzoate daily for periods of four to eighteen days to 16 patients with hyperpiesia. Their observations were carefully controlled and appeared to show that when given by mouth it had no effect on the raised pressure in hyperpiesia.

We submitted benzyl benzoate to a trial in 30 patients with hyperpiesia, and observed its effect in a daily dosage of 24 minims (1.6 mils) during 45 test periods. A fall occurred during 7 test periods, conspicuous in 3 and moderate in 4; there was no change during 23; and a rise took place during 15, conspicuous once and moderate in 14 instances.

Symptomatic improvement was recorded during 15 test periods, but during 30 the symptoms either remained stationary or became worse.

A comparison of these results with those obtained from placebo treatment is made in Table VI.

TABLE VI

COMPARING THE EFFECTS OF CALCIUM CHLORIDE, ATROPINE SULPHATE, POTASSIUM THIOCYANATE, AND BENZYL BENZOATE WITH THOSE OF A PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure Value			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Calcium chloride ..	25 (43)	18 (32)	54 (58)	28 (10)	24 (37)	76 (63)
Atropine sulphate ..	9 (30)	12 (42)	64 (46)	24 (12)	33 (33)	67 (67)
Potassium thiocyanate	90 (88)	37 (36)	40 (50)	23 (14)	34 (31)	66 (69)
Benzyl benzoate ..	45 (61)	16 (39)	51 (48)	33 (13)	33 (34)	67 (66)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

SOME VEGETABLE EXTRACTS

Guipsine.—This is a preparation of mistletoe which has been advocated on account of its alleged action as a vasodilator of the peripheral arterioles.

Guipsine was tried in 12 patients with hyperpiesia, and its effect observed in a daily dosage of 9 pills during 19 test periods. A fall occurred during 6, conspicuous in 1 and moderate in 5; there was no change during 9; and a rise took place during 4, conspicuous once and moderate in 3 instances.

Symptomatic improvement was recorded during 4 test periods on guipsine, but during 15 the symptoms either remained stationary or became worse.

Detensyl.—This consists of extracts of mistletoe, liver, pancreas and lung; and because a hypotensive action from vasodilatation has been ascribed to each of these constituents it has sometimes been recommended.

We submitted detensyl to a trial in 14 patients with hyperpiesia, and observed its effect in a daily dosage of 4 tablets during 18 test periods. A fall occurred during 4 test periods, conspicuous in 1 and moderate in 3; there was no change during 9; and a rise took place during 4, conspicuous in 1 and moderate in 3. One patient failed to take the tablets.

Symptomatic improvement was recorded during 6 test periods on detensyl, but during 12 the symptoms either remained stationary or became aggravated.

Phyllosan is the name given to a concentrated extract of chlorophyll obtained from green vegetables. Originally recommended in the treatment of anæmia, it has recently been accredited with hypotensive effects, but on such meagre evidence that we accepted it into our series for additional control observations.

We submitted phyllosan to a trial in 9 patients with hyperpiesia, and observed its effect in a daily dosage of 6 tablets during 16 test periods. A moderate fall occurred during 4; there was no change during 9; and a rise took place during 2 test periods, conspicuous in one and moderate in another. The effect could not be recorded in one patient because he was unable to take this medicine on account of giddiness.

Symptomatic improvement was recorded during 5 test periods, but during 11 the symptoms either remained stationary or became worse.

Citrin (cucurbocitrin).—Barksdale (1926) isolated an active principle from the seed of the water-melon which belongs to the group of glucoside-saponins and which prove on experiment to dilate the smaller arteries. Barksdale claimed good results in 10 cases of nephritic hypertension. In 68 patients in whom the blood pressure was raised, Wilkinson (1927) found a fall with symptomatic improvement in 82 per cent. Cucurbocitrin was given by Althausen and Kerr (1929) in daily doses of 150 to 450 mg. to 40 patients with hypertension. An immediate fall in pressure was noticed and its extent appeared to be directly dependent on the dosage. After prolonged administration an average fall of 29 mm. in the systolic and of 15 mm. in the diastolic pressure occurred in 73 per cent. of the cases, while symptomatic improvement was recorded in even more; toxic symptoms were never noted. Gargill and Rudy (1931) treated 29 cases of hyperpiesia with cucurbocitrin and found it of no value; in only 7 instances was the systolic pressure reduced by 25 mm., a reduction which might occur spontaneously. Seward (1931) prescribed it in 16 patients in doses varying from 150 to 200 mg. daily. The blood pressure was reduced in 4 after treatment for fourteen days, and this effect lasted for some time and went with symptomatic improvement. Later he (1932) reported that in 9 out of 22 cases the systolic pressure was reduced by 30 mm. and the diastolic by 10 mm. following treatment with citrin in doses of from 300 to 400 mg. daily.

We submitted citrin to a trial in 13 patients with hyperpiesia, and observed its effect in a daily dosage of 300 mg. during 13 test periods. A fall occurred during 2 test periods, conspicuous in 1 and moderate in 1; there was no change during 7; and a rise took place during 2, conspicuous in 1 and moderate in 1. In 2 instances the patients were unable to continue taking the medicine.

Symptomatic improvement was recorded during 4 test periods on citrin, but during 9 the symptoms either remained stationary or became aggravated.

Toxic effects, namely headache, insomnia and a sense of choking, occurred in 3 instances.

Yohimbine, an alkaloid obtained from yohimbine bark, is a peripheral vasodilator, and produces a small hypotensive effect. It is said to augment the action of other agents, and Loeper and Lemaire (1930) found that in dogs previously treated with yohimbine, the hypotensive effects of acetylcholine were four times as great. Barrieu (1932) reported good results from such a combination when given to patients. Taken with phenylethyl-barbituric acid it was favoured by Busquet and Vischniac (1935).

We submitted yohimbine hydrochloride to a trial in 16 patients with hyperpiesia, and observed its effect in a daily dosage of $\frac{1}{3}$ grain (0.02 g.) during 18 test periods. A moderate fall occurred during 3 ; there was no change during 6 ; and a moderate rise took place during 5. In 4 instances the patients could not continue taking the drug.

Symptomatic improvement was recorded during 4 test periods on yohimbine, but during 14 the symptoms either remained stationary or became worse. Toxic effects, namely trembling, shivering, dizziness, and headache, occurred in six instances.

SOME ANIMAL EXTRACTS AND HORMONES

Padutin, originally known as kallikrein, is a pancreatic extract. It is alleged to contain a vasomotor hormone with hypotensive properties when given either by mouth or by intramuscular injection, and it is standardized by physiological methods. A fall in blood pressure was observed by Leschke (1930) in patients with hyperpiesia when taking padutin. In some the fall was considerable and persistent, while in others it was slight and transient. Scharpff (1931) compared the effects on the blood pressure of rest and a restricted diet, with and without padutin. A fall in pressure occurred in both groups, but was more noticeable in those taking padutin, where the average fall in the systolic and diastolic values was 64 and 31 mm. as against an average fall of 35 and 5 mm. in patients not taking padutin. Subjective improvement was also recorded. Nuzum, Elliot, and Bischoff (1937) gave kallikrein hypodermically in ten patients ; they controlled their results and found a fall in pressure in only two patients while the symptoms remained unchanged. Wolffe and others (1937) observed the effects of de-insulinated pancreatic extract in 150 patients with hypertension. A fall in systolic and diastolic pressure occurred in 108, and in 8 of these it was conspicuous ; symptomatic improvement was noticed in 62 per cent. and lasted for over twelve months. In the remaining 42 the changes were comparable with those observed in a control series.

We submitted padutin to a trial in 36 patients with hyperpiesia, and observed its effect in a daily dosage of 60 minims (3.6 c.c.) during 46 test periods. A fall occurred during 9 test periods, conspicuous in 5 and moderate in 4 ; there was no change during 21 ; and a rise took place during 16, conspicuous in 5 and moderate in 11.

Symptomatic improvement was recorded during 17 test periods on padutin, but during 29 the symptoms either remained stationary or became aggravated.

Vagotonine is obtained from the pancreas, and its specific physiological action is said to be one antagonizing the action of adrenaline and restraining its secretion ; through its action on the sympathetic system it reduces vasomotor tonicity. Abrami, Santenaise, and Bernal (1933) recorded a fall in the blood pressure in 42 of 80 cases of hypertension after subcutaneous injections of 20 or more often 40 mg. of vagotonine. If a fall did not occur within two hours of the first injection, they did not expect any reduction from daily injections even when repeated on twenty consecutive days ; on the other hand, the fall which commenced within two hours was maintained from 12 to 48 hours. Urticaria was sometimes seen.

We observed the effects of a subcutaneous injection of 0.02 g. of vagotonine in 6 patients with hyperpiesia, and in one of these the injection was repeated. Frequent blood pressure readings were taken before and after the injection for a period not less than two hours, and further readings were recorded on subsequent days. We also had evidence of the variation in the blood pressure value during periods of treatment with active drugs or placebo mixtures. In none of our 6 patients was the blood pressure lowered, either immediately or more remotely, by injections of vagotonine and indeed it was at a higher level after the injection in 4 of them. We concluded that vagotonine had no place in the treatment of hyperpiesia, for in the patients in whom it was given a trial it produced no hypotensive effects. In one patient it gave rise to very severe urticaria.

Angioxyl is an insulin-free extract of pancreas which is standardized physiologically. It has been claimed that it antagonizes the action of adrenaline and that it produces vasodilatation, resulting in a lowering of the blood pressure.

We submitted it to a trial in 10 patients with hyperpiesia, and observed its effect in a daily dosage of 80 units during 15 test periods. A fall occurred during 5, conspicuous in 3 and moderate in 2 ; there was no change during 5 ; and a rise took place during 4, conspicuous in 2 and moderate in 2. In one instance the patient had failed to take the medicine on account of headache.

Symptomatic improvement was recorded during 5 test periods on angioxyl, but during 10 the symptoms either remained stationary or became aggravated.

Bioglan H consists of a concentration of hormones obtained from pancreas, anterior pituitary and human placenta. In 20 cases of hypertension selected from the druggist's laboratory files it is recorded that an average blood pressure of 210/117 before treatment became 158/91 after treatment, and this reduced value had persisted for a year after the initial course of injections.

One c.c. of bioglan H was injected intramuscularly twice weekly for three weeks in four female patients with hyperpiesia, and for two weeks in a male patient. Daily blood pressure readings were taken under controlled conditions and when these were considered it was found that in no instance had it caused any reduction.

A comparison of the results of these preparations and of anabolin with those obtained from placebo treatment is made in Table VII.

TABLE VII

COMPARING THE EFFECTS OF 8 PREPARATIONS WITH THOSE OF A PLACEBO ON THE BLOOD PRESSURE AND ON THE SYMPTOMS IN PATIENTS WITH HYPERPIESIA

Drug	Number of Test Periods	Change in Blood Pressure			Effect on Symptoms	
		Fall	No Change	Rise	Improved	Not improved or worse
Guipsine	19 (24)	30 (28)	50 (64)	20 (8)	21 (40)	79 (60)
Detensyl	18 (38)	24 (37)	53 (52)	23 (11)	33 (37)	67 (63)
Phyllosan	16 (13)	26 (24)	60 (69)	14 (7)	33 (46)	67 (54)
Citrin	13 (29)	18 (31)	64 (52)	18 (17)	29 (35)	71 (65)
Yohimbine hydrochloride	18 (42)	21 (23)	42 (61)	37 (16)	22 (33)	78 (67)
Padutin	46 (75)	20 (32)	45 (59)	35 (9)	37 (34)	63 (66)
Angioxyl	15 (20)	33 (45)	41 (35)	26 (20)	34 (25)	66 (75)
Anabolin	35 (52)	18 (24)	61 (61)	21 (15)	20 (27)	80 (73)

Figures, excepting those in the first column, denote percentage of test periods. Figures in brackets apply to placebo.

Anabolin is an extract of liver isolated by alcohol fractionation methods, and its introduction into clinical medicine in the treatment of hyperpiesia has depended on its specific action as a vasodilator. Its pharmacological action in lowering blood pressure in the experimental animal is constant and uniform, so that solutions containing it can be standardized by this method. Major (1924 and 1925) appeared to show that hypertension could be induced experimentally by the introduction of guanidine bases, and because he was able to reduce this rise by the administration of liver extract he postulated that its hypotensive action did not depend solely on vasodilatation, but that it also assisted the liver in destroying pressor bodies in the form of amino-acid waste products. Later (1926) in 100 patients with hypertension he reported that an immediate fall in the blood pressure could be obtained from liver extract injections, and that this effect was often conspicuous and lasted for several hours. MacDonald (1925) gave the results obtained from the treatment of 33 patients with hyperpiesia. Lautman (1926) reported a fall in blood pressure in 34 cases of hypertension following 10 to 24 daily injections of liver extract. Harrower (1926) recorded a fall in blood pressure in 40 cases of hypertension from the use of anabolin (1 to 4 tablets daily) by mouth. Burnett (1926) expressed his opinion that the hypotensive effects of liver extract depended mainly on the histamine which it contained, and in 1929, with Althausen and Kerr, he described favourable results from the use of intramuscular injections in 27 cases with hypertension. Willis (1930) has described the preparation and standardization of anabolin and has stated that it is free from choline and that histamine is only present in negligible quantities. When used intravenously in 150 cases of hyperpiesia it invariably lowered the blood pressure and produced symptomatic improvement, but the same favourable results were not obtained from its oral administration.

We submitted anabolin to a trial in 22 patients with hyperpiesia, and

observed its effect in a daily dosage of 3 tablets by mouth during 35 test periods. A fall occurred during 6, conspicuous in 3 and moderate in 3 ; there was no change during 20 ; and a rise took place during 7, conspicuous in 4 and moderate in 3. In 2 instances the effects could not be recorded because the patients failed to continue taking anabolin on account of dizziness.

Symptomatic improvement was recorded during 7 test periods on anabolin, but during 28 the symptoms either remained stationary or became aggravated.

Sex Hormones.—Steinach, Peczenik, and Kun (1938) investigated the action of male hormone preparations on male patients with hypertension, and noted a fall in the systolic pressure in 31 of 49 cases treated with androsterone benzoate or testosterone propionate. Symptomatic improvement also took place. In a further series small doses of œstradiol benzoate were added to the male hormone. They found that cases which proved refractory to the male hormone alone responded favourably to the combined preparation. Steinach and Kun (1937) believed that the male hormone was converted into an œstrogenic substance when injected into male patients, and they attributed clinical improvement in male patients with hypertension to the converted male hormone.

Perandren (male hormone) and œstrone (female hormone) were given consecutively by intramuscular injections of 1 c.c. twice weekly for three weeks in 8 patients with hyperpiesia, 4 of whom were males and 4 females. Frequent blood pressure readings were recorded, and comparing these with those obtained during control periods on a placebo mixture we concluded that neither preparation evoked any hypotensive effect.

WEIGHT-REDUCING DIET IN HYPERPIESIA

Embleton (1938) recorded a steady and lasting fall in blood pressure in 18 patients with hyperpiesia while taking a high-protein diet which caused reduction in the body weight. He mentioned, however, that transitory rises in the pressure took place on account of constipation or severe emotional strain. His claims were based on a comparison of subsequent blood pressure readings with the initial reading. The present investigation has convinced us of the necessity of discarding the first and sometimes even the second reading in order to avoid the fallacious deductions which inevitably result if these are accepted as values standard for the patient. In 28 out of 64 unselected cases of hyperpiesia in this series we found that the blood pressure at the second examination after placebo treatment did not vary by more than 10 mm. from that recorded at the first examination, but in 36 cases a variation of more than 25 mm. had occurred ; in 9 it had risen and in 27 it had fallen. Not only did a fall take place three times more often than a rise, but the extent of the fall was much greater than the rise ; thus only 3 cases showed a rise exceeding 40 mm. and none exceeded 60 mm., whereas among the 27 cases where a fall had taken place it was 40 mm. or over in 11 cases and in 5 of these it was 60 mm. or over.

We determined the effects of a reducing diet in 5 patients with hyperpiesia and obesity during a period when no active drugs were prescribed. The daily diet, providing for equal values of protein, fat and carbohydrate, had a calorie value of about 1168 calories, and was made up as follows :

Breakfast : Tea with milk. Two eggs or a piece of fish or one thin rasher of bacon. Vita-weat biscuit. Butter (size of a cherry). Tomatoes or fresh fruit (4 lb.).

Dinner : A good portion of lean meat or cheese. Plateful of green vegetables or salad. One small apple, orange, pear, or grapefruit. Vita-weat biscuit.

Tea : Tea with milk. One egg. Vita-weat biscuit and butter (size of a cherry).

Supper : A fair portion of steamed fish or lean meat or cheese. Plateful of green vegetables or salad. Vita-weat biscuit and butter (size of two cherries). One small apple, orange, pear, or grapefruit.

Sugar, cakes, pastries, puddings, jam, bread, potatoes, bananas, and fried food were not allowed.

A satisfactory reduction of body weight was always obtained within a short period and details of this and the blood pressure readings have been set out in charts (Figs. 3, 4, 5 and 6). When these results were compared with

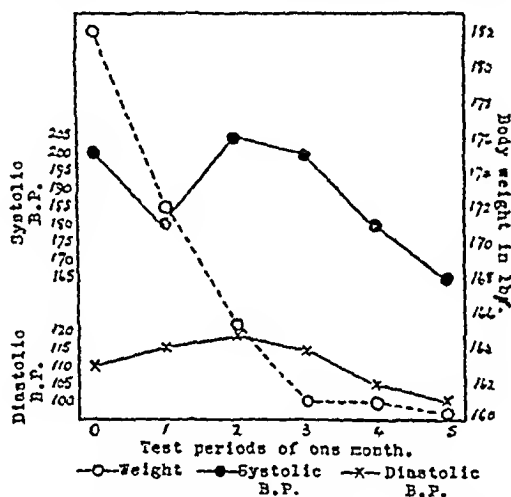


FIG. 3.—Blood pressure in a female, aged 59, with hyperpiesia, during treatment with a fat-reducing diet.

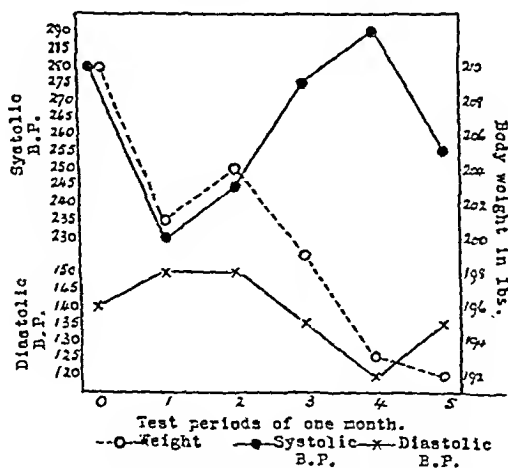


FIG. 4.—Blood pressure in a female, aged 53, with hyperpiesia, during treatment with a fat-reducing diet.

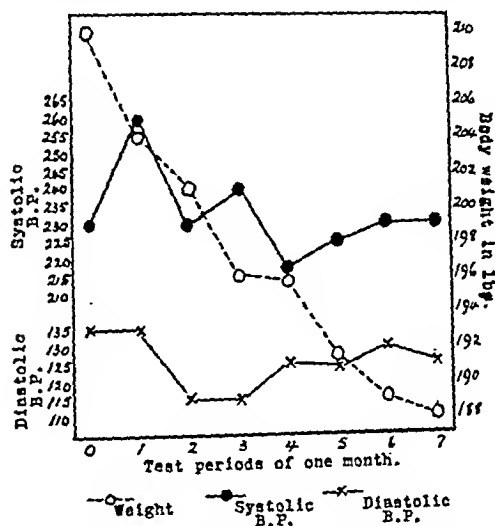


FIG. 5.—Blood pressure in a female, aged 48, with hyperpiesia, during treatment with a fat-reducing diet.

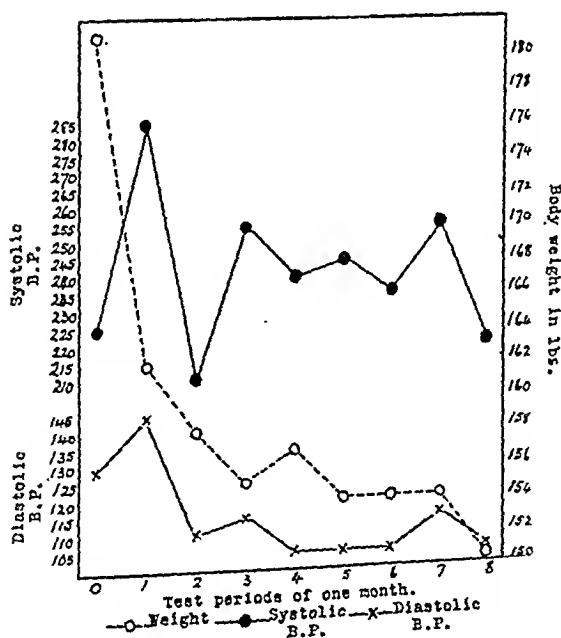


FIG. 6.—Blood pressure in a female, aged 68, with hyperpiesia, during treatment with a fat-reducing diet.

those obtained from the use of a placebo only (Fig. 1), we concluded that dietetic treatment which effected a considerable reduction in the body weight did not influence the blood pressure in patients with hyperpiesia, although symptomatic improvement from loss of weight usually took place. During the period when the weight was falling quickly and later when the reduced weight was being maintained the blood pressure showed a variation which we have come to regard as a normal occurrence in a patient with hyperpiesia (Fig. 1). Observations in these five obese patients undergoing dietetic treatment have in this way provided us with another opportunity of watching this natural variation.

DISCUSSION OF RESULTS

Natural Variation in Blood Pressure

Although we knew that the blood pressure fluctuates from time to time, becoming higher during periods of nervousness, as this investigation proceeded we came to realize more fully how great is the natural variation and how false would be the judgment of the hypotensive action of a drug if this were ignored. No drug should be credited with such properties unless it has exerted this effect to a greater extent than that which occurs naturally during a period on placebo treatment. Fig. 1 shows these periodic changes in the blood pressure during a time when a placebo medicine was the only form of treatment. Similar variations are seen in Figs. 2 to 6 in patients on a reducing diet and a placebo.

Again, the initial blood pressure, i.e. the first reading, is often so much higher than the standard for the individual patient that a disregard of this fact has led to a wrong estimate of the hypotensive properties of certain drugs. Thus among those patients in whom a second reading differed from the first by more than 25 mm. while on placebo treatment there was a fall in three-quarters of the cases. Frequently the systolic value fell 40 mm. and often more than 60 mm. (see Table VIII). We attributed the higher initial readings to the

TABLE VIII

CHANGE IN THE BLOOD PRESSURE AT THE SECOND EXAMINATION WHEN TAKING A SIMPLE PLACEBO MIXTURE

Data	Blood Pressure Change		
	No Change or Change of less than 10 mm.	Rise	Fall
Sixty-four patients with hyperpiesia	28	9	27
Change in systolic blood pressure in mm.	—	15 15 25 20 20 15 40 45 50	20 15 25 25 20 15 15 25 25 20 20 20 25 15 25 20 50 60 75 40 40 40 65 65 60 45 45

excitement at the first clinical examination, and sought confirmation of this by recording the pressure continuously in 7 healthy subjects and in 7 patients with hyperpiesia until it assumed a constant and basic level as they rested on the examining couch. The extent of the fall and the time taken to reach this level is shown in Table IX. The effect of emotional disturbance on the blood

TABLE IX

THE FALL IN BLOOD PRESSURE TO ITS BASIC LEVEL WITH REST ON AN EXAMINATION COUCH.
THE BLOOD PRESSURE WAS RECORDED EACH MINUTE

Case	Initial State of the Blood Pressure	Extent of Fall of Systolic Pressure in mm. before reaching a Constant Basic Level	Time (in minutes) taken to reach Basic Level
1	Raised	20	6
2	Raised	55	19
3	Raised	30	5
4	Raised	5	2
5	Raised	10	6
6	Raised	10	4
7	Raised	10	7
8	Normal	20	20
9	Normal	15	2
10	Normal	30	9
11	Normal	5	1
12	Normal	25	6
13	Normal	10	4
14	Normal	10	10

pressure was next observed in patients at rest and just after a verbal explanation about amyl nitrite inhalation. A rise in the blood pressure invariably took place and within two minutes of the explanation (Table X and Fig. 7). Such changes are of obvious importance in considering the effect of a drug.

TABLE X

THE RISE OF SYSTOLIC BLOOD PRESSURE AFTER EXPLAINING THE DETAILS CONNECTED WITH AMYL NITRITE INHALATION

Case	Initial State of the Blood Pressure	Extent in mm. to which the Systolic Blood Pressure Rose within Two Minutes of the Explanation
1	Raised	25
2	Raised	10
3	Raised	25
4	Raised	10
5	Raised	10
6	Raised	5
7	Raised	10
8	Normal	20
9	Normal	20
10	Normal	30
11	Normal	25
12	Normal	15
13	Normal	15
14	Normal	35
15	Normal	15

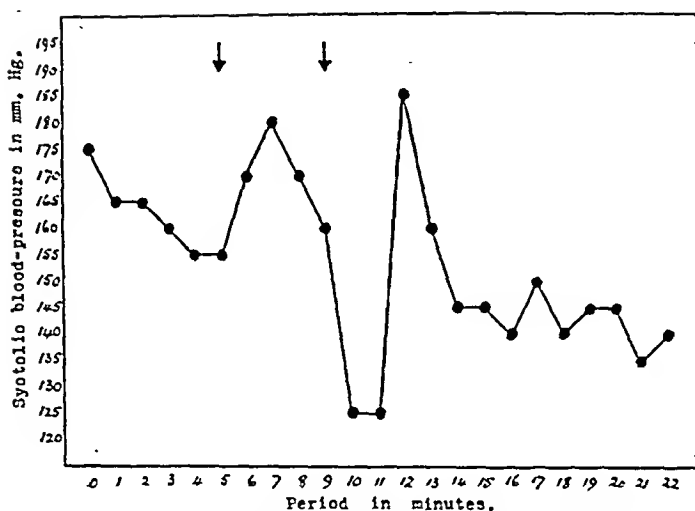


FIG. 7.—Showing the reaction of the blood pressure to emotional disturbance and to inhalation of amyl nitrite. The blood pressure, which has taken four minutes to fall to its basic level, rises following an explanation of the procedure of amyl nitrite inhalation, falls abruptly after the inhalation, and maintains a low level following a temporary and reactionary rise. The first arrow in the chart indicates the stage at which the explanation was made and the second arrow denotes the time of the inhalation.

Effect of Drugs on the Blood Pressure

Not until our records were completed did we examine the results critically, and then it was apparent that although these patients had been taking continuously the many reputed remedies none showed any clinical change nor any effective fall in blood pressure. It never assumed a value during treatment with any of the 33 remedies tried that was lower than the value recorded in the same patient when an inert placebo was exhibited. It is remarkable that even when considered statistically (see Table XI) in terms of hypotensive effects estimated from the relative incidence of the fall and rise in blood pressure while taking the different remedies, papaverine sulphate and chloral hydrate were the only two drugs producing collective results a trifle better than an inert placebo, and not enough to justify their routine use in hyperpiesia. No evidence was obtained to justify the prescribing of any of the tested preparations if the object is to reduce the blood pressure, for it has been shown here that none of them possesses this property under clinical conditions. The indiscriminate use of new and often expensive remedies for hypertension without first submitting them to a *controlled* clinical trial is to be deprecated.

Effect of Drugs on Symptoms

The effects of a blood pressure variation were watched particularly where a rise or fall of more than 25 mm. had taken place. During 64 test periods when this conspicuous change was a rise the symptoms improved in 36 per cent., were unchanged in 38 per cent. and were worse in 26 per cent. During 90 test periods when the change was a fall the symptoms improved in 34 per cent., were unchanged in 46 per cent. and were worse in 20 per cent. The symptoms in a patient with hyperpiesia, therefore, bear no relation to the height of his blood pressure at the time. It caused some surprise to find no improvement in such a high proportion of patients when the pressure had fallen conspicuously, and it caused greater surprise to find improvement in symptoms coinciding with a rise as often as with a fall in the blood pressure.

TABLE XI

SUMMARIZING THE CHANGES IN BLOOD PRESSURE IN PATIENTS WITH HYPERPIESIA DURING TEST PERIODS WHILE TAKING DIFFERENT MEDICINES

Medicine	Number of patients	Number of Test Periods each of 14 days	Change in Blood Pressure (expressed as percentage of the test periods)		
			Fall	No change	Rise
PLACEBO	59	131	28	52	20
Sodium nitrite	19	22	14	43	43
Glyceryl trinitrate	11	11	28	15	57
Erythrol tetranitrate	13	19	36	32	32
Mannitol hexanitrate	24	29	36	23	41
Bismuth subnitrate	22	39	20	44	36
Potassium iodide	23	28	14	68	18
Iodine	20	42	10	67	23
Potassium bromide	40	66	32	44	24
Sodium luminal	38	52	27	50	23
Chloral hydrate	23	33	30	55	15
Papaverine sulphate	16	24	34	54	12
Euphyllin	31	41	27	56	17
Diuretin	26	30	20	64	16
Theominal	16	21	23	53	24
Doryl	11	12	12	50	38
Pacyl	11	22	18	68	14
Hypotan	19	36	27	45	28
Calcium chloride	20	25	18	54	28
Atropine	9	9	12	64	24
Potassium thiocyanate	38	90	37	40	23
Benzyl benzoate	30	45	16	51	33
Guipsine	12	19	30	50	20
Detenzyl	14	18	24	53	23
Phyllosan	9	16	26	60	14
Citrin	13	13	18	64	18
Yohimbine hydrochloride	16	18	21	42	37
Padutin	36	46	20	45	35
Angioxyl	10	15	33	41	26
Anabolin	22	35	18	61	21

An estimate was made of the symptomatic improvement gained by patients under treatment with the various remedies. The improvement was always assessed by a comparison with progress shown during test periods on a placebo. Improvement greater than that shown during placebo treatment was only found in six of the active drugs, bismuth subnitrate, iodine and iodide, bromide, sodium luminal, theominal and potassium thiocyanate. Excepting bismuth subnitrate, they only proved slightly superior to a placebo. In patients manifesting nervousness, restlessness and sleeplessness, bromide, sodium luminal and theominal often ameliorated the symptoms, but without any associated effect on the blood pressure.

SUMMARY AND CONCLUSIONS

The effect of 33 preparations on the blood pressure and symptoms was watched in 70 patients with hyperpiesia (essential hypertension) over a period of eighteen months. The drugs or preparations were various and included nitrites, iodides, sedatives, xanthine and choline derivatives, vegetable extracts and hormones. Naturally it was not possible to test each remedy in every patient as some were accepted after the investigation had begun and a few failed to complete the whole course. Each medicine was prescribed in optimum doses for test periods of a fortnight, and at the end of each period the patient attended for re-examination, when the blood pressure was recorded under the same unvarying and standard conditions and any change in symptoms was noted.

When the basic pressure for each patient had been estimated from the first three observations, the hypotensive effect (or absence of effect) of a particular drug was often decided in individual patients at the end of a test period of 14 days, but as a rule each drug was given a second trial over longer intervals in a certain number of patients. To begin with, and later at irregular intervals, control test periods were instituted for each patient, when an inert placebo mixture was the only treatment given. In two patients the blood pressure was recorded throughout the investigation while taking a placebo of which the colour and flavour were the only variants. In five obese patients it was recorded while on a reducing diet and without drugs.

After allowance had been made for the tendency to obtain high blood pressure readings at the first and possibly at the second examination, and for the natural variation, and when the results from the tested drugs were compared with those from a placebo, we found that none of the 33 preparations produced hypotensive effects in patients with hyperpiesia. In regard to symptomatic improvement, only 6 of the drugs, namely bismuth subnitrate, iodine and iodide, bromide, sodium luminal, theominal and potassium thiocyanate, on an average relieved symptoms rather more than did the placebo. The sedative drugs seem to have value in temporarily relieving nervous symptoms when these were prominent.

Although these results may surprise some, they will accord with the expectation and experience of many physicians. Admittedly, this paper deals with only a small section of the therapeutics of hyperpiesia, and it does not bear on the management of hypertensive heart disease including heart failure, where drug treatment can often be seen at its best. Our negative findings with drugs in uncomplicated hyperpiesia do not make it less desirable that the patient should remain under medical supervision. It is obvious that a patient should not regard his symptoms as closely related to the height of his blood pressure. Medical attention must be devoted to the alleviation of symptoms when they arise and to correcting faults in living, and particularly to the adoption of timely active measures when symptoms or signs of heart failure first appear.

Time will show whether surgical measures are a practicable means of lowering blood pressure and of lessening symptoms in hyperpiesia. Meantime a clearer insight into the origin of hypertension must precede its successful treatment with drugs.

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ELECTROCARDIOGRAPH ELECTROLYTES

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The contact with the body needed for electrocardiographic purposes is often made by wrapping a few layers of gauze soaked in saline round the limb and binding over that a metal electrode. This method has the disadvantages that the limb to limb resistance is rather high and increases considerably as the gauze dries. Also the bedclothes must be protected from becoming wet when an electrocardiogram has to be taken from a bedridden patient.

If the limb to limb resistance is high the string of the Einthoven galvanometer must be slackened to increase the sensitivity, and so the record may be distorted by the alteration of the damping and the reduction of the natural frequency of the string (Pardee, 1917). In the case of valve electrocardiographs, with their high input resistance—usually about 100 times that of the string—high body resistance is not so disadvantageous; but if it can be kept low there is less likelihood of electrical interference, and in addition the stability of the amplifier is increased.

We were led to consider these points recently while carrying out some cardiac tolerance tests by a method described previously (Bell and Knox, 1938). As some of our experiments lasted more than an hour the drying of the saline pads was a great handicap. We therefore tried soft green soap, as used by Boas (1928) under similar circumstances, and found that it fitted our requirements admirably.

Although skin resistance has often been investigated in connection with chronaxie and the psychogalvanic reflex, we could find no report of a systematic investigation into the properties of electrolytes, apart from the work of Hartridge (1931) which dealt with the effect of grease-removing substances. It was thought, therefore, that it would be interesting to compare soft green soap with certain other electrolytes.

METHOD

The electrolytes investigated were :

1. One per cent. sodium chloride in tap-water.
2. Soft green soap (Sapo Mollis Viridis, B.P.) which consists chiefly of an almost neutral mixture of potassium oleate with a little glycerine.

3. Cambridge electrode jelly, which is sold by the Cambridge Instrument Co. ; the composition of this substance is not issued.

4. A paste described by Jenks and Graybiel (1935), which we shall call for convenience Boston paste ; it consists mainly of sodium chloride, glycerine, water, and powdered pumice.

In the case of the first electrolyte, two layers of gauze bandage soaked in saline were wrapped round the forearms. Plymet electrodes each 14 cm. by 5 cm. were laid on the volar surfaces and held in place by rubber bands. Plymet is a soft sheet metal (supplied by Schall and Son, New Cavendish St., London, W.1), consisting mainly of lead, which is readily moulded to the shape of the arm.

In the case of Cambridge jelly a piece of the jelly about the size of the fingernail was rubbed into the forearms for about ten seconds, as recommended by Russell (1935). The Plymet electrodes were then smeared with the jelly, put directly on the skin, and held in place with bandages and rubber bands. The soft green soap and Boston paste were applied in a similar manner.

As is well known, there are some quick changes (rise and fall of R wave) and some slow changes (T wave) in the electrocardiogram. Hence an adequate description of the behaviour of an electrolyte should include both the D.C. resistance and the A.C. impedance.

The measurements were made by means of a bridge in which the subject formed one arm, and a variable resistance with a variable capacitance in parallel formed the second arm ; the ratio arms were formed by two equal resistances of 1000 ohms. Alternating current was supplied to the bridge by a valve oscillator which gave about 8 volts at 300 cycles per second (c.p.s.). A sensitive vibration galvanometer tuned to 300 c.p.s. was used to find the balance condition. The values of resistance and capacitance in the second arm, combined vectorially, gave the A.C. impedance, Z .

$$\text{Thus } Z = \frac{r}{\sqrt{1 + \omega^2 C^2 r^2}}, \text{ where } \omega = 2\pi f.$$

When the A.C. measurement had been made, an 8-volt battery was substituted for the oscillator and a moving coil galvanometer for the vibration galvanometer and the bridge brought once more to balance by varying the resistance in the second arm. This gave the direct current resistance, R .

RESULTS

The wide scatter of the results, which are collected together in Fig. 1, is not altogether surprising in an experiment of this nature. As it was not, of course, possible to get simultaneous values for the different electrolytes, they were applied in turn, varying the order with each subject.

The values of Z were distributed over a considerable range. One per cent. sodium chloride gave, on the whole, the lowest values (average 652 ohms), Boston paste gave slightly higher values (average 689 ohms), whilst green soap and Cambridge jelly both gave still higher values (average 768 and 754 ohms respectively).

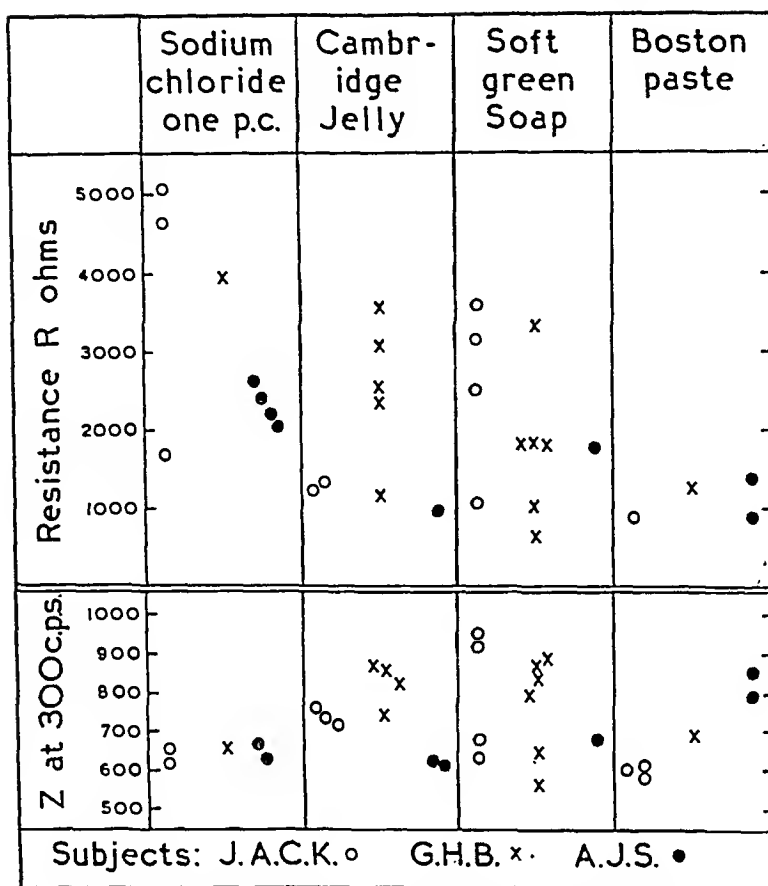


FIG. 1.—Chart of all the observations of body resistance from forearm to forearm for the three subjects with the four different electrolytes.

R was found to be highest with 1 per cent. sodium chloride, the average value being 3080 ohms. Cambridge jelly and green soap gave the somewhat lower average values of 2010 and 2040 ohms respectively. Boston paste gave the lowest average resistance of 1100 ohms.

In order to allow of further discrimination between the solid electrolytes, variation of R and Z with time was investigated. The electrodes were left in position for varying times up to one and three quarter hours and Z and R, in that order, were measured at quarter-hour intervals. The leads were removed from the bridge between readings. In all cases Z and R rose steadily, but not very greatly, for about three quarters of an hour after application of the electrodes, when the values became nearly constant (see Fig. 2).

DISCUSSION

From the wide scatter of the results shown in Fig. 1 it will be seen that it is not at all easy to choose the best electrolyte on the basis of Z and R values only.

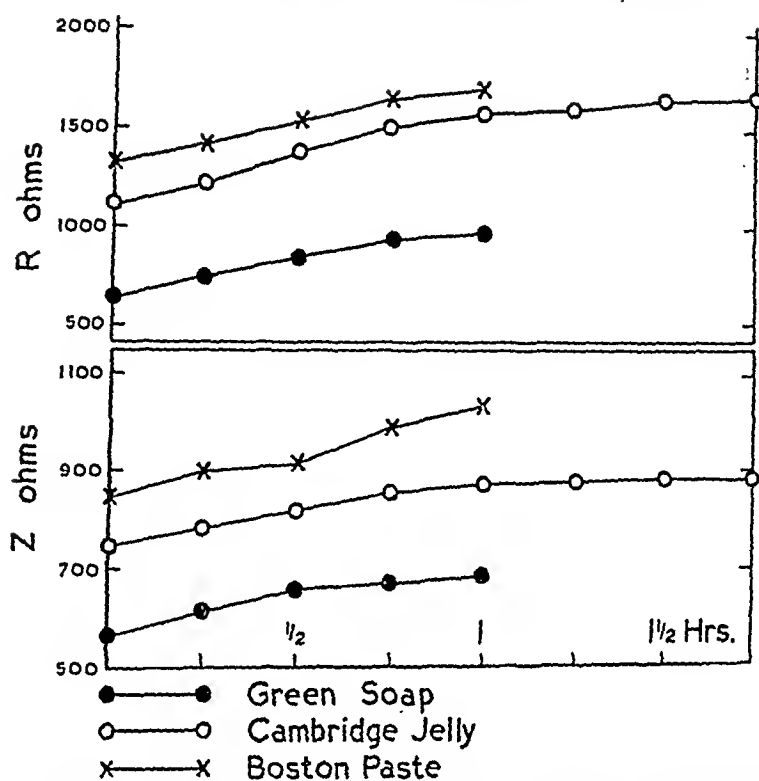


FIG. 2.—Variation of resistance (forearm to forearm) with time. Cambridge jelly and Green soap, subject G. H. B., Boston paste, subject A. J. S.

The best is probably Boston paste. Green soap and Cambridge jelly are only slightly inferior; sodium chloride, on account of its very high R , is the poorest.

Drying up of the solid electrolytes does not occur to any great extent because none of them show any great increase in resistance up to one hour or more after application. There was no difference between electrocardiograms taken by means of a string galvanometer using first green soap and then Cambridge jelly. The choice between the three solid electrolytes will, therefore, have to be made on other grounds.

As green soap is a standard British Pharmacopœial substance and costs only about one penny per oz., it is to be preferred to the complicated Boston paste or the expensive Cambridge jelly.

THE EFFECT OF ABRASIVES

Boston paste is made up with a considerable proportion of powdered pumice, which at first we regarded merely as an inert base required to form the paste. But examination of Cambridge jelly points to a different conclusion. It appears to consist chiefly of sodium chloride in a base which is probably not lanoline or petroleum jelly, but which may be a gum. The jelly feels gritty to

the touch, and on dissolving away the base in hydrochloric acid an insoluble residue remains, which under the microscope proves to consist of extremely jagged particles of crushed quartz.

It is now clear why the jelly should be rubbed into the skin ; the sharp particles remove the surface cells and so contact is made with a deeper layer. Richter (1926, *a* and *b*) showed that a minute puncture of the skin below electrodes one inch square reduced *R* from 540,000 ohms to 15,000 ohms. Lewis and Zotterman (1927) came to the conclusion that the high resistance displayed by skin to galvanic currents resided in the superficial and horny layer. Accordingly it was decided to investigate the effects of abrasion quantitatively.

METHOD AND RESULTS

To one sample of green soap we added pumice in the proportion occurring in Boston paste and to another sample crushed quartz recovered from Cambridge jelly.

In these experiments the average value with green soap alone for *Z* was 885 ohms and for *R* was 2450 ohms. After rubbing in green soap with quartz the average values were *Z* 665 ohms and *R* 890 ohms, a decrease of 25 per cent. in *Z* and 64 per cent. in *R*. Rubbing in green soap with pumice left *Z* unchanged but reduced *R* by 57 per cent. Green soap covers the quartz and pumice particles and interferes with their abrasive qualities. It occurred to us, therefore, that it would be more effective to abrade the dry skin and then apply the electrolyte and electrode. The surface of the skin was rubbed gently two or three times with fine glass paper (No. 1). This raised the surface layer of cells so that the skin lost its sheen and became white in colour. This procedure resulted in a reduction of *Z* by 60 per cent. and of *R* by 80 per cent. on the average, the mean values after such abrasion being : *Z*, 400 ohms, and *R*, 500 ohms, approximately. These are the lowest values which we have observed during the whole course of this investigation.

In addition to the alteration of *Z* and *R* brought about by abrasion, it was noted in measuring *Z* that the resistive component required for balance fell to about one-half, or less, of the value before abrasion. The capacitance in parallel, however, fell to about one-tenth. For example, in one experiment before abrasion the bridge was balanced by 1790 ohms in parallel with 0.386 mfd., i.e. $Z=1090$ ohms ; after abrasion, balance was given by 368 ohms in parallel with 0.035 mfd., i.e. $Z=368$ ohms.

DISCUSSION

From the above results there is no doubt that if the lowest possible body resistance is required, gentle abrasion of the dry skin with glass paper, followed

by application of green soap and then of the electrodes is the most convenient method. Provided the rubbing is gentle and only two or three strokes are used, the skin will return to its normal appearance in a few hours. In our experience there is nothing objectionable in making this a routine procedure, provided that no irritating antiseptics, such as iodine, are applied afterwards. Only one minor difficulty appeared; it is rather hard to use glass paper on hairy parts, because the hairs roll round under the paper and no abrasion of the skin is made. This could be overcome by removing the hairs before abrasion. It was found that more vigorous glass papering, or scratching, which left a mark taking over a week to disappear, did not give lower values than the more gentle method.

By the use of the procedure recommended above the external resistance (i.e. of the patient) becomes a much smaller fraction of the resistance of the galvanometer, which should then be expected to give a better record of the potentials occurring in the patient's body. Also, when the patient's resistance is low the electrocardiograms obtained should be more standard, as even relatively large alterations of this resistance will then have little effect on the total resistance of the circuit. We have found that in the case of the A.C. bridge the capacitance value (without abrasion) varies from 0.15 to 0.5 mfd., using the same electrodes. It is difficult to predict what would be the effect of this capacitance on the electrocardiogram. The effect on damping of capacitances across the string has been studied by Gildemeister (1922). Here again, however, more standard results would be expected when the capacitance is low, as is the case when the skin is abraded, because the variations in the capacitance then become of small importance. It was also noted that when the skin was abraded the values of R and Z tended to be very steady, whereas without abrasion there was a tendency to drift.

It is interesting to speculate how far the differences which are occasionally found between records taken by string and valve electrocardiographs are dependent on high patient resistance and impedance. There seems to be a tendency to regard records taken by a string galvanometer as standard, in spite of its relatively low resistance. This tendency seems to be based more on tradition than on pure reason. It would be interesting to compare string and valve electrocardiograms in a series of cases taken with the technique described here. We venture to think that with the low patient resistances so obtained a number of the discrepancies would disappear. This question has already had some attention directed to it by Pardee (1929).

Variations in the Quality of the Green Soap.—During the course of these experiments we had occasion to purchase three separate samples of Sapo Mollis B.P. The first sample was soft, bright green in colour, and spread very easily and evenly over the skin surface. The second sample was harder, dark green in colour, very tenacious, and became caked when rubbed on the skin, refusing to spread evenly. The following figures show that this second sample was inferior to the first for our purposes. The values for R were usually over 10,000 ohms, and the average value for Z (11 observations) was 915 ohms, compared with the averages R 2040 ohms and Z 768 ohms for the first sample.

The third sample of Sapo Mollis was comparable in every way with the first, and in obtaining it the following criteria were observed. The green soap must be *fresh* and should be *bright* green in colour, and it should spread as easily on the skin as a good ointment base. It should be kept in an air-tight tin or waxed carton.

The difference in effectiveness was not due to a change in the resistance of the soap. The specific resistance of the second sample (tough soap) was 18.4 ohms per cm. cube; the value for the third sample (good soap) was 23.9 ohms per cm. cube. It is to be presumed that the lowering of skin resistance with the good soap is due to the fact that it spreads so easily and evenly over the skin.

SUMMARY

Reasons are given for the necessity of having a low limb to limb resistance when obtaining electrocardiograms either by the string galvanometer or by a valve electrocardiograph.

A comparison has been made between four electrolytes, viz. 1 per cent. sodium chloride, soft green soap, Cambridge electrode jelly, and Boston paste (Jenks and Graybiel, 1935).

The arm to arm D.C. resistances (R) and impedances at 300 cycles per second (Z) vary over a wide range for all these electrolytes. From this point of view the best is probably Boston paste, but Cambridge jelly and soft green soap are very little inferior.

Because it is cheap, clean, simple, and a standard pharmacopœial product soft green soap appears to be the most satisfactory. It should be fresh, bright green in colour, and should spread easily over the skin.

Both the Boston paste and the Cambridge jelly contain abrasives. Incorporation of an abrasive in the green soap reduced the average values of resistance and impedance to a moderate extent.

The lowest values of limb to limb resistance (R, 500 ohms; Z, 400 ohms) were obtained when the abrasion preceded the application of the electrolyte as follows: the dry skin was stroked gently two or three times with fine glass-paper, green soap was then applied and the electrodes were bound on.

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SIR JAMES MACKENZIE'S HEART

BY

DAVID WATERSTON

WITH AN ACCOUNT OF HIS CLINICAL HISTORY BY JAMES ORR, AND NOTES ON
THE PATHOLOGICAL HISTOLOGY BY D. F. CAPPELL.

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The following description of Sir James Mackenzie's heart has been prepared in accordance with his desire, expressed to myself and to other friends, that after his death his heart should be examined to ascertain what information it furnished upon the symptoms that he had experienced. He died in London on January 25, 1925, aged 72. Some weeks before his death he told Dr. John Parkinson that he wished him to make a post-mortem examination. This request was confirmed, after his death, by his brother, Sir William Mackenzie, now Lord Amulree. The examination was performed, some fourteen hours after his death, by Dr. John Parkinson, assisted by Dr. J. W. Linnell. The heart was removed and subsequently sent to me at St. Andrews for further examination. Dr. Parkinson noted that nothing abnormal was found in the pericardium.

In order to correlate the clinical symptoms with the pathological condition, it has been necessary to compile an account of Sir James Mackenzie's illness. This has not been easy for, like so many other doctors, he had not been under the care and observation of a medical man from the commencement of his illness. His own case is referred to both in his book on angina pectoris (Case No. 28) and in that on diseases of the heart, as well as in the Reports of the St. Andrews Institute.

While he was in London, from 1908 to 1918, he mentioned to Sir Thomas Lewis that his anginal history began suddenly. While he was in St. Andrews, from 1918 to 1924, engaged in founding the Institute for Clinical Investigation which bears his name, he was on many occasions examined by Dr. James Orr, and discussed with him his condition. Dr. Orr also saw him during several of the attacks of angina, from which he suffered with increasing severity as the years went on. After his return to London in 1924 he was not under the care of any medical man until very shortly before his death, when he was seen by Dr. Parkinson and Dr. C. M. Anderson.

Dr. Orr, who had seen him during the whole of his stay in St. Andrews, has written the account of the clinical history which follows. My colleague, Professor D. F. Cappell, undertook the histological examination of the blood vessels and heart muscle, and his notes on them are included in the description.

CLINICAL HISTORY AT ST. ANDREWS

The medical life history of Sir James Mackenzie is the story of the onset and gradual progress of angina pectoris from sclerosis of the coronary arteries. He had a mild attack of typhoid fever in 1880 and an occasional attack of renal colic in his later years, but suffered from no other illness.

With the exception of a tendency to extrasystoles commencing at the age of forty, the first evidence of real cardiac involvement was in 1901, at the age of forty-seven. This was a heart attack with irregularity of the pulse, which occurred after running 300-400 yards. In his own description of this attack (Mackenzie, 1925) he notes that he "was conscious of a slight fluttering sensation, but suffered no distress of any kind." The pulse rate during this attack, which lasted two hours, was 90 per minute. A tracing, taken by himself, showed auricular fibrillation. During the next four or five years several attacks of this kind occurred, mostly after a full meal or when walking up a hill; they lasted from ten minutes to half an hour and never caused any distress or limitation in his powers of walking.

The earliest symptom of limitation of effort was noticed by himself in 1907, and was represented by a slight feeling of constriction, hardly amounting to pain, in the upper part of the chest on severe continued exertion, and which soon ceased with rest. There were long periods when it was not experienced at all. For two years he was conscious of slight pain on effort under certain conditions, such as walking after a full meal or on a cold day. This pain he described as preceded by a sense of tightness or constriction, such as used to pull him up when running a race in boyhood.

In 1908, at the age of 55, Mackenzie experienced his first severe attack of cardiac pain. It occurred at night when resting, and followed a period of dining out at frequent intervals. The pain was across the chest and down the left arm; it lasted two hours and varied in severity. Mackenzie further notes that in this attack "he could not be still but had to move about." After 10 grains of veronal sleep was obtained, and next day he was quite well and free from pain, though walking in the cold or after a meal still produced discomfort of an anginal type. This gradually became more noticeable, and by 1911 there was definite limitation of effort, though pain could be avoided by careful regulation of effort. From this time until the end of his life a somewhat anomalous symptom was present, to which he often referred, namely, that while a sustained effort produced pain, a sudden effort produced breathlessness without pain.

Mackenzie came to St. Andrews in 1918, and at that time was able to walk

at any pace from his home to the Cottage Hospital without discomfort, a distance of two miles. In 1919, when I first examined him, he was still able to do this and could play a round of golf regularly. The heart was then $1\frac{1}{4}$ inch external to the mid-clavicular line, the sounds were closed and well spaced, and, except for an occasional extrasystole, the rhythm was regular. Blood pressure was 156/92 mm. At this time he was also affected with intermittent claudication on continuous walking. He had first noticed this ten years previously after a rapid four-mile walk, but in 1919 it was evident after a short half-mile walk. The posterior tibial pulse was well felt on both sides. During the next five years this symptom was much less pronounced owing to the fact that pain in the chest occurred in response to a smaller effort than was necessary to produce claudication.

In 1922 limitation of effort prevented his playing golf, and even walking became difficult though by careful regulation of effort, severe pain was, in the main, avoided. A few very severe attacks occurred, like that in 1908, while resting. The most severe of all, in 1923, happened while he was sitting in his study in the afternoon, and lasted nearly an hour; it was little influenced by nitroglycerine and was followed by extreme exhaustion. In August 1924 Mackenzie returned to London, and by this time only the gentlest of exercise was possible. Death followed a very severe and prolonged anginal attack in January 1925. As has been already mentioned, Dr. John Parkinson saw him shortly before his death, and has supplied the following note:

"On January 24 and 25, 1925, he suffered severe and prolonged attacks of anginal pain, and Dr. C. M. Anderson was called during the night. At 4.30 a.m. on January 25 he had morphine subcutaneously, gr. $\frac{1}{2}$, and chloroform inhalation for about an hour. It was necessary to repeat both at 8.20 p.m. on that day. At this time the pulse was 100 and regular and there was Cheyne-Stokes breathing. I did not myself see him until 10.30 p.m. that night (January 25), and he was then asleep. About 1 a.m. on January 26 he awoke free from pain and perfectly conscious and composed. He conversed cheerfully with Lady Mackenzie and me for a few minutes and then said he felt sleepy and soon he slept. At 4 a.m. his breathing changed and became irregular with long pauses, and a few minutes later the pulse stopped. There were no indications of pain at the end."

EXAMINATION OF THE HEART

The heart was uniformly enlarged. Its weight was 18 oz. (510 g.) and it measured 14 cm. transversely, 13 cm. vertically and 28.5 cm. in circumference at the base of the ventricles. It should be mentioned that Mackenzie was a tall man of powerful physique, in whom a heart above the average size would be expected.

There was a considerable amount of sub-epicardial fat, especially in the right A-V sulcus, along the right border, and in the anterior interventricular

furrow. The epicardium was smooth and nowhere thickened. The veins on the surface of the heart were distended and more prominent than usual. On the anterior surface, numerous small vessels passed from the inter-ventricular furrow towards the left border, anastomosing with small vessels there, and these in turn with branches of a medium sized vessel on the inferior surface.

The right auricle, was dilated. Its wall was thin and, between the bundles of the pectinate muscles, translucent. The opening of the coronary sinus was large. The crista terminalis and the valve of the inferior vena cava were prominent. The tricuspid orifice and valve were of normal size and showed no pathological changes.

Microscopical Examination.—In longitudinal section the wall measured 7.5 mm. in thickness, of which the outer 6 mm. was chiefly adipose tissue containing a few scattered muscle bundles showing atrophic changes supervening on previous hypertrophy. In the outer fatty layers several small non-medullated nerve bundles were present, together with a few groups of sympathetic nerve cells. In the inner part of the wall the muscle bundles were more closely packed, the individual fibres were hypertrophied, and some showed atrophy and degeneration with increase of fibrous stroma between the fibres.

In transverse section the appearances were of a similar nature and indicated a considerable degree of ischaemic atrophy and fibrosis of some duration. There was no evidence of recent infarction, and foci of inflammatory infiltration were absent throughout the sections.

The right ventricle was large, its muscular wall rather thin, pale in colour and in places almost yellowish. There was no evidence of fibrosis of the wall. At the base of the infundibular portion, where the inner surface was smooth, the muscular coat was 6 mm. in thickness, while about the middle of the cavity, where papillary muscles were present, it measured 16 mm., of which more than half was sub-epicardial fat. The pulmonary valve was normal in structure and competent.

Microscopical examination of the papillary muscles.

(a) The sections showed a portion of papillary muscle on transverse section with a central arterial twig accompanied by a small nerve bundle. At one side was an area of adipose tissue separated from the endocardium by thin fibrous layer at one side and by a few muscle bundles at the other. The fibres of the papillary muscle were hypertrophied, but there was no increase of fibrous tissue and no evidence of old or recent infarction.

(b) The longitudinal sections of papillary muscle showed essentially similar features: marked infiltration of adipose tissue, hypertrophy of the muscle bundles and, in one group of sections, a mild degree of ischaemic fibrosis towards the attached end of the papillary muscles.

The arterial twigs in the papillary muscle had slightly thickened walls but their lumina were not narrowed.

The left auricle measured 7 cm. in diameter, both transversely and vertically. Its wall was thin and measured only 2.5 to 3 mm. in thickness. The mitral orifice admitted two fingers and the valve was competent. The marginal cusp was



FIG. 1.—Section of the wall of the left ventricle near the apex, showing a recent small hæmorrhagic infarction, involving the deeper part of the muscle wall, covered by a nodular reddish-brown mass of clot, the size of a cherry-stone, projecting into the cavity of the ventricle

short and its surface nodular, especially near the attached margin. It was incompletely divided into three portions. It measured 6 cm. along its base and 17 mm. from the base to the free margin. The aortic cusp was, as is usual, much larger, and measured 24 mm. from its attached to its free margin. It showed no evidence of pathological changes.

The left ventricle was a large and thick walled chamber. The muscular wall, for the most part thick and firm, was 27 mm. in thickness near the base. At the apex, as usual, it was thin, and only 3 mm. in diameter. In colour it was somewhat pale. In its substance were several small whitish patches of fibrous tissue, in size from a pin's head upwards. In the anterior wall, 30 mm. above the apex, there was a patch of fibrous tissue 8 by 3 mm. and another patch of similar structure and size lay in the substance of the posterior wall, about midway between apex and base. At the apex there was a small recent hæmorrhagic infarction involving the deeper part of the muscle wall, covered by a nodular reddish brown mass of clot the size of a cherry stone which projected into the cavity of the ventricle (Fig. 1). Section through this and the adjacent wall showed that the nodular tissue extended into the substance of the muscular wall, which was here reduced to a narrow margin 3 mm. thick.

Microscopical examination.—The section comprised the whole thickness of the ventricular wall. The muscle fibres in the outer layers were greatly hypertrophied and the interstitial tissue was of about normal amount. In the inner half the fibres showed a much greater degree of ischæmic fibrosis and irregularly shaped fibrous scars were numerous, in which muscle fibres in all stages of atrophy were found. The section did not contain any large branch of the coronary arteries and the smaller branches included showed a little thickening of their muscular coats, but no noteworthy intimal change.

The section of the infarction showed a portion of the apex of the left ventricle, the endocardium being partly covered with thrombus both old and recent. The muscle fibres were in general much hypertrophied, but there was a rather severe patchy ischæmic fibrosis which had produced marked thinning of the ventricular wall at the apex. On the internal aspect there was severe subendocardial fibrosis with many muscle fibres undergoing atrophy and degeneration and over this area there was a mass of old thrombus, decolorized in the centre and showing an early stage of organization. The greater part of the thrombus, however, was of recent coralline type and was well preserved, being only loosely attached to the wall. Between the thrombus portions of the columnæ carneæ were seen to be the seat of ischæmic fibrosis with fatty and vacuolar degeneration of the surviving fibres.

The apical myocardium did not show any sharply defined infarctions, but just at the apex there were several patches of more intensely eosinophile fibres whose nuclei appeared to be pyknotic and degenerate. Between these fibres there was a considerable degree of leucocytic infiltration which extended into the overlying epicardial fat. The small blood vessels in the fat were dilated and engorged with blood. None showed any evidence of thrombosis. It is probable that the areas of altered staining reaction and leucocytic infiltration were in a condition of early infarction.

The aorta had been divided 6 to 7 cm. from its root. At the point of division the lumen was cylindrical, measuring 33–34 mm. The ascending aorta showed a bulging to the right side (the bulb of the aorta) by which the

diameter was increased to some 45 mm. The interior of the ascending aorta showed extensive yellow mottling in patches, some separate and some discrete, 3-4 mm. in diameter. Near the root the mottling formed an arborescent pattern. The surface of these mottled areas was slightly raised. In thickness the wall measured 3.5-4 mm., but in places it measured 6 mm. On the posterior wall of the interior of the aorta was a large yellowish raised patch beginning about 35 mm. from the root of the aorta and extending beyond the level at which the vessel had been cut. In this area there was very considerable thickening of subintimal tissue and the tunica intima readily separated off from the other coats. The root of the aorta showed comparatively little pathological change. There were small thin yellow patches of atheroma round the root of the right coronary artery and adjacent to the orifice of the left coronary artery, but the lumen of these vessels was not materially narrowed. Except for the large area mentioned, the wall of the aorta was pliable and showed no general pathological alteration, there being only slight subintimal atheroma.

Section of the patches on the wall showed atheromatous changes of the intimal and subintimal coats. External to the smooth endothelium of the intima was a firm, pale yellow layer some 3 mm. in thickness; external to this the darker coloured and almost unchanged tunica media. There was little, if any, calcification in the subintimal thickenings.

Microscopical Examination.—The aortic wall was greatly thickened by a large atheromatous patch which measured 1.5 mm. in thickness. External to this the

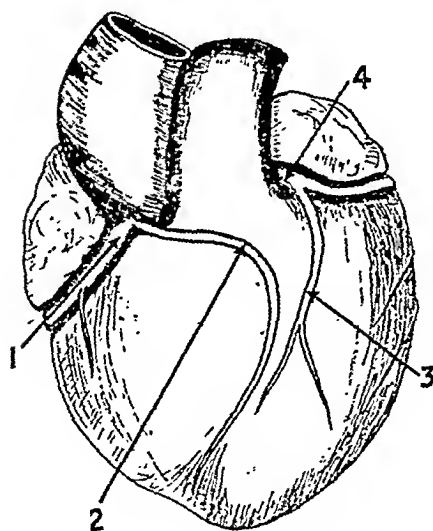


FIG. 2.—Arrangement of the coronary vessels on the anterior surface of heart.

(1) Stem of right coronary artery. (2) Interventricular branch of right coronary artery. (3) Interventricular branch of left coronary artery. (4) Left coronary artery.

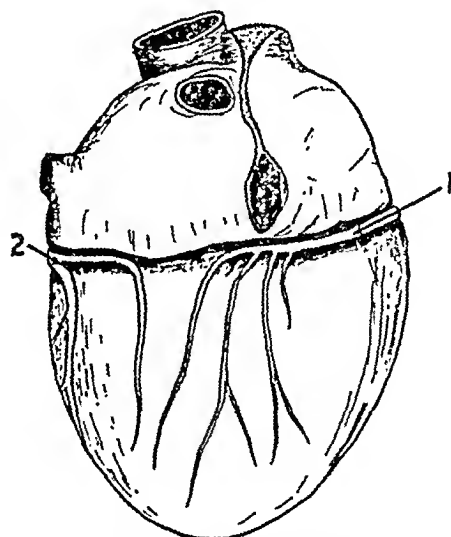


FIG. 3.—Arrangement of the coronary vessels on the inferior surface of heart.

(1) Right coronary artery. (2) Left coronary artery.

medial coat measured 1.15 mm. in thickness. The atheromatous lesion was of the usual type, consisting of degenerate fatty and granular material, with masses of foamy cells and also areas of clefts resulting from fatty crystals. In places the atheromatous lesion involved the innermost part of the media, with foamy cells between the musculo-elastic layers and degenerative changes in the inner elastic laminæ and muscle fibres. The middle coat was a little hypertrophied and in the outer part the tissue elements were comparatively healthy; inflammatory cellular infiltration was absent and the elastic laminæ were intact.

Coronary arteries.—Both of the arteries and their branches were the seat of advanced and widespread degenerative changes, which had caused thickening of the wall of, especially, the medium-sized and smaller vessels, and diminution of their lumen. The arteries most affected were those in the anterior ventricular furrow, of which there were two, one from each coronary stem. These vessels were so thickened and calcified that their lumen was almost obliterated. A recently occluded vessel was not found as a cause for the infarction mentioned above.

Right coronary artery.—Near its root the external diameter of this vessel was 9 mm. Its wall was greatly thickened and the lumen, oval in outline, measured 2 by 3.6 mm. The thickening involved mainly the subintimal coat and also the tunica media, and the wall was firm and rigid. Section of the wall showed patches of degenerated cheesy material in the centre of the thickened areas, and the changes involved almost the whole circumference of the vessel.

From near the root of the artery a branch, 4 mm. in diameter, passed in the anterior interventricular sulcus to the inferior margin, lying by the side of a slightly larger branch from the stem of the left coronary artery. The two vessels ran side by side in the anterior longitudinal furrow, the left one giving a superficial branch and then entering the muscular coat half-way down, while the right artery ran onwards superficially. The wall of both of these vessels was greatly thickened, and the lumen in each reduced to a minute capillary cleft.

Half an inch from its root the diameter of the right coronary artery was 8 mm. At this point the thickening was less pronounced and the lumen wider. The artery continued as a large vessel and gave off numerous branches; a small branch in the epicardial fat along the right margin; a very tortuous branch which ran on the inferior surface an inch from the right margin; a small vessel to the base of the ventricle; at the left portion of the coronary sulcus three branches to the inferior surface of the ventricle, arising close to one another and measuring 2–3 mm. in diameter; finally, the terminal portion of the artery turned downwards in the inferior interventricular sulcus. The distal portion of the artery showed much slighter pathological change, the lumen, though diminished, being distinct.

Histological Examination

(a) *Stem of the right coronary artery* (Fig. 4).—The artery was greatly enlarged, the maximum diameter being 7.5 mm., owing to confluent patches of atheroma which surround the lumen and produced irregular narrowing. Adjacent to the lumen there was a thick subendothelial layer of hyaline connective tissue beneath which at one side there was a large crescentic patch of dense calcification, 3.5×2 mm., extending as far as the junction with the media, the muscular layer of which was thinned and atrophied. At the other side of the vessel the intima was fully 3 mm. in thickness and consisted chiefly of degenerate and granular material throughout which there are clefts left by dissolving out of fatty crystals. Foci of calcification were present in this material here and there. Red blood cells had seeped into the degenerate material in places and were seen in well preserved state in the superficial part of the atheromatous lesion. The medial coat of the artery was thin and atrophied. The adventitia had been largely stripped off during dissection. A small arterial twig seen leaving the parent vessel was practically unaffected by atheroma. There was no evidence of thrombosis in this portion.

(b) *More distal portion*.—This portion of the vessel measured 5 mm. in greatest diameter and was concentrically thickened, the lumen measuring 2 mm. The thickening was due chiefly to increase of the intima, which consisted of hyaline connective tissue with pronounced patchy granular and fatty degenerative changes in the deepest layers next to the media. These showed the usual cleft-like spaces where fatty crystals had been removed and there were several patches of calcification, the largest measuring 1.25 mm. in diameter. The media showed atrophy of the muscular layers which were reduced to a mere trace over the larger calcified patches. At the junction between media and intima there were, at several places, clusters of wide, thin-walled vessels filled with red cells and around these a mild round-celled infiltration. These appeared to be reactive, newly formed vascular channels, and from them a few thin-walled capillaries extended into the hyalinized layers of the thickened intima. The adventitial coat had been largely stripped off in dissection, but where present showed no evidence of inflammatory reaction. The lumen of the vessel was free from thrombus.

(c) *Ventricular branch*.—The vessel was smaller but showed similar though less severe change. There was again widespread atheroma, but the lumen was not so greatly reduced and there was an absence of the calcification so prominent at the higher level. The sections were not quite complete, a portion of the media being missing from one side in all sections. At one side the atheromatous intimal lesion consisted largely of foamy cells with patches of degeneration devoid of cellular structure, and at one point the surface had broken down and a small atheromatous ulcer had formed. This appeared to be very recent, as there were foamy cells mingled with fresh blood corpuscles in the lumen, but there was no evidence of thrombus formation over the damaged area. The tunica media was somewhat atrophied, but there was no noteworthy fibrosis. The adventitia showed no lesion.

(d) *Interventricular branch* (Fig. 5).—The artery was thickened, measuring 4×3 mm., and the lumen was eccentric and was reduced to a mere crescentic slit 1×0.3 mm. Opposite the convexity the intima was occupied by two large patches of very degenerate atheroma showing abundant fatty clefts and granular material. These patches had become confluent and both were surmounted by a mass of hyaline connective tissue. The larger patch showed much calcification of its outer portion next to the media. Opposite the convexity of the lumen the intima was thickened by multiple layers of hyaline stroma, without fatty degeneration in the deeper layers, and around the lumen the connective tissue was more loose and cellular and its arrangement suggested a recent formation indicative of arterial closure such as occurs in endarteritis from diminished blood flow.

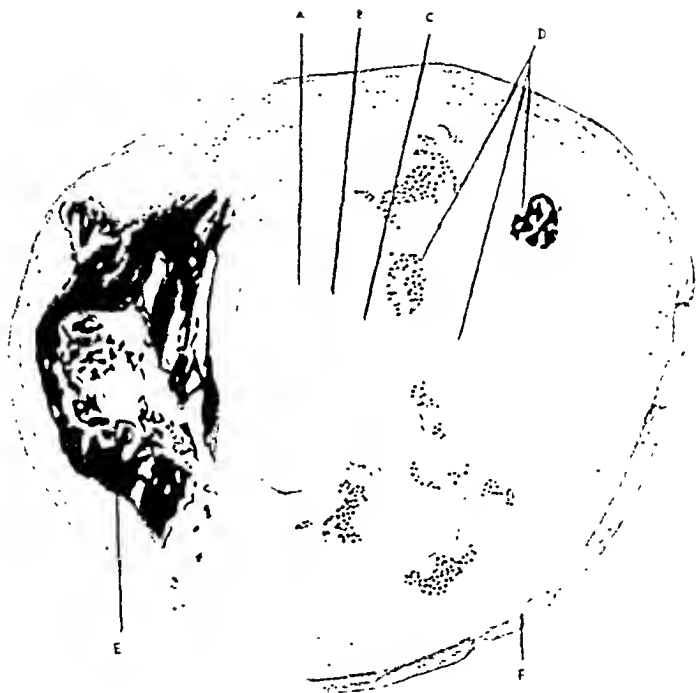


FIG. 4.—Section of the stem of the right coronary artery, showing the lumen irregularly narrowed by thickening of the sub-endothelial and middle layers, and patches of degeneration and calcification.

(A) Lumen. (B) Endothelial tunic. (C) Sub-endothelial tunic. (D) Patches of degeneration and calcification in middle tunic. (E) Large calcified area. (F) Adventitial tunic.

The media was much thinned and atrophied and overlying the larger calcified intimal patch there was complete disappearance of the muscular layer. A few wide, thin-walled vessels of newly-formed type were seen between the media and intima

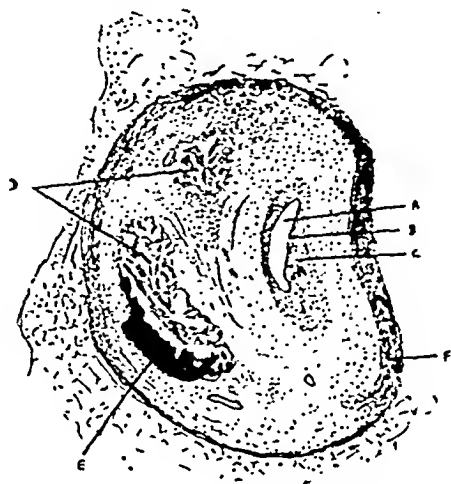


FIG. 5.—Section of interventricular branch of right coronary artery.

(A) Lumen. (B) Endothelial tunic. (C) Sub-endothelial tunic. (D) Patches of degeneration. (E) Calcified patch. (F) Adventitial tunic.

surrounded by round cells and a few foamy macrophages. In the adventitial coat there were several patches of round-cell infiltration, chiefly lymphocytes; plasma cells did not appear to be present.

The left coronary artery was smaller than the right, and its wall was less affected by pathological change. The external diameter at the root was 6 mm. and the wall not more than 1 mm. thick. It gave off a large branch already mentioned to the anterior interventricular furrow; the wall of this branch was more affected pathologically than the stem of the artery, there being marked intimal thickening in patches near the root, while an inch or two distally the thickening was even more pronounced, involving the whole wall and reducing the lumen to an extremely small size. The left coronary artery gave a large branch to the left margin of the heart. The wall of this branch too was distinctly thickened, and in the more distal portion so thickened as to reduce the lumen to the smallest dimensions.

(a) *Marginal branch* (Fig. 6).—The section showed a portion of cardiac muscle and one large artery and two small branches, the largest vessel measuring 3 mm. in diameter. The lumen was reduced to an eccentric elongated slit 1.6×0.065 mm. in diameter. At one side the intima was occupied by a large patch of degenerate atheroma consisting of granular material and clefts of fatty crystals with much calcification in the deeper layers. External to this area the media was almost totally destroyed and there was an abundant formation of new capillary vessels widely dilated and thin walled, between the deeper part of the intima and the media and at one point replacing the muscular wall completely. This newly-formed vascular tissue was

filled with round cells and macrophages, many of which were packed with dark brownish pigment which gave the Prussian blue reaction for iron. Similar cells were present in abundance in the adventitial coat overlying the lesion. The appearances suggested that there had been an interstitial hæmorrhage which had become organized

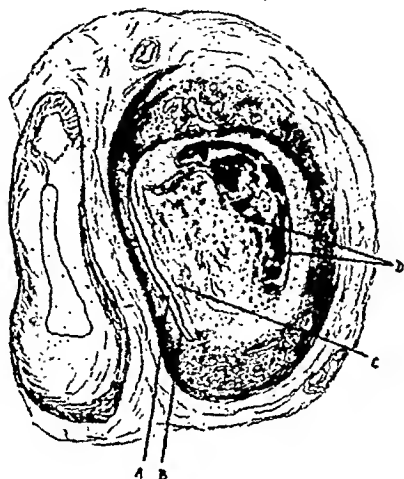


FIG. 6.—Section of marginal branch of left coronary artery, showing the diminished slit-like lumen and a large patch of degenerate atheroma, destruction of the media, and newly-formed vascular tissue replacing the muscular wall. Two smaller vessels show moderate sub-intimal thickening but absence of atheromatous disease.

(A) Lumen. (B) Endothelial tunic. (C) Sub-endothelial tunic. (D) Degenerated and calcified patches in middle tunic.

and repaired. The two smaller arterial branches showed a moderate degree of subendothelial intimal thickening, with musculo-elastic hyperplasia, but atheromatous disease was absent.

(b) *The interventricular branch* measured 3.2 mm. in diameter, the lumen, eccentric and almost circular, measuring 1.0 mm. The thickening was again due to severe atheroma, two patches showing marked degeneration and calcification being confluent, while less pronounced atheromatous deposits were also present on the opposite wall. The media was much thinned over the calcified patches, being almost devoid of muscular tissue.

There was also a minor degree of new capillary formation between media and intima and in several places thin walled capillaries had penetrated some distance into the degenerate intima and could be seen between the degenerate fatty patches and the subendothelial hyaline layer, which was, however, completely avascular.

The adventitial coat showed only a single small focus of round-cell infiltration and was devoid of pigment bearing macrophages.

Summary of Condition of Vessels

Both coronary vessels and their branches showed extensive and far-advanced sclerosis in the form of patchy thickenings of the wall, which in some instances diminished and practically obliterated the lumen.

THE CONDITION OF THE HEART IN RELATION TO THE SYMPTOMS

(1) The first signs of heart impairment occurred in 1908, seventeen years before his death, when he experienced a sharp attack of severe pain, which with our present knowledge would be diagnosed as due to a coronary thrombosis. There is evidence in the heart to confirm this view, for the patch of fibrosis near the apex corresponds to the structural damage which would be caused by such an attack.

Sir Thomas Lewis, who was good enough to send me his opinion after examining the heart, wrote to me as follows :

“ Grant and I examined the heart very closely and we are agreed that there are amply sufficient old-standing changes at the apex of the heart to account for the first attack of pain described in his case notes. That attack of pain is strongly suggestive of coronary thrombosis, and the fibrosis at the apex is distributed in a way that also suggests thrombotic obstruction of an apical branch.”

(2) The severe atheroma of the coronary arteries and their branches, with diminution of the lumen, affords ample cause for the occurrence of attacks of cardiac pain. Both of the arteries were affected and the anterior interventricular branch of each was greatly narrowed.

(3) There were numerous small patches of cicatrization in the substance of the muscular wall of the left ventricle. These patches though smaller were of the same nature as the larger fibrous patch at the apex, which was due to thrombosis of an apical branch. Other arteries to the left ventricle were profoundly altered and their lumen narrowed. This has been shown for example in the marginal artery of the left ventricle. There would therefore appear to have been numerous small thromboses at different times, each of which would be accompanied by symptoms similar to those experienced at the first attack. Several such attacks are recorded and the similarity is brought out in the case history. It is noted, for example, that on many occasions the attacks came on during rest and were quite unrelated to effort.

(4) The presence of numerous small blood vessels on the surface of the heart points to there having been an opening up of small vessels and the establishment of at least a partial anastomotic pathway for the supply of blood to the areas most severely impaired by the attacks of thrombosis. In this connection it may be remarked that during the last few months of his life between August 1924 and January 1925, Sir James's condition showed slight improvement. I found, for example, that not only could he walk for some distance down Exhibition Road from his home in Albert Hall Mansions, but he was able to walk up that road without distress, though at a slow pace. This improvement doubtless was due to a slight improvement, by anastomosis, in the arterial supply to the heart.

(5) The terminal severe attack of pain and cardiac impairment was associated with the occurrence of the recent infarction found at the apex of the left ventricle.

(6) There was no evidence of any impairment in the valves or in the genetic

system of the heart. The impairment was entirely in the muscular wall, brought about by the atheromatous disease of the arteries.

We have to thank Miss M. H. Kidston for preparing illustrations 1-6.

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CARDIAC MYXOMA

A CLINICAL AND PATHOLOGICAL STUDY

BY

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Received April 12, 1939

We wish to place on record this case of so-called cardiac myxoma because it appears that only rarely do descriptions of this interesting lesion appear in British publications. We have found only one British reference during the last nine years, the case of Gilchrist and Miller (1936) which will be discussed later in this paper ; on the other hand, numerous references have appeared during the last few years in America and Germany. The lesion is a rare one, much less common than the appearance of secondary neoplasm. The latter were found by Welch (1931) in 0.22 per cent. of autopsies, and Ward (1934) reports a corresponding figure of 0.3 per cent., whereas Lymburner (1934) states that primary neoplasms of the heart were found in 0.05 per cent. of autopsies, of this number 75 per cent. were innocent and the majority of innocent tumours were myxomas.

DESCRIPTION OF THE CASE

A woman aged 60 was admitted for the first time to the City General Hospital, Leicester, on March 4, 1938, with the diagnosis of diabetes mellitus and bronchitis. She had previously complained of rheumatic pains in the shoulders and since 1925 she had had various attacks of epigastric pain and vomiting. More recently it had been known that her blood pressure was above the normal. During her stay in hospital her diabetic condition was readily stabilized, nothing abnormal was discovered in her cardiovascular system except slight hypertension, B. P. 170/90 mm., and she was discharged after fifteen days.

Almost immediately after returning home she began to suffer from fainting attacks, but on no occasion was she seen by her medical attendant whilst in an attack. Præcordial pain also occurred and was associated with marked dyspnœa and some cough. Præcordial pain and dyspnœa now continued until December 1938, when diarrhœa started. This symptom became so pronounced that the patient was readmitted to hospital on January 14, 1939, for investi-

gation. No abdominal lesion could be found to account for this symptom and no abnormal physical signs were found in the heart other than slight left ventricular hypertrophy. Her diabetes had remained controlled and she appeared to be in satisfactory health until January 18, when for the first time in hospital there was a complaint of faintness and dizziness which was considered to be a mild attack of hypoglycæmia. A similar attack occurred five days later, and this responded immediately to a hypodermic injection of adrenalin. On the evening of January 28 she had a very severe attack without any previous warning, and when seen she was pulseless and was thought by the sister of the ward to be dead. An injection of 15 minims of adrenalin was given into the left ventricle and 3 c.c. of coramine were injected intravenously. Within two minutes the pulse could be felt at the wrist and the patient recovered consciousness and began to talk.

On auscultation of the heart it was found to be fibrillating and it continued to fibrillate for about 3 minutes before normal rhythm was resumed. The patient appeared quite comfortable for an hour, then, again, without warning, she collapsed; 15 minims of adrenalin were given into the heart and again the patient, who had for a second time been pulseless, recovered, became a good pink colour and was able to talk. She remained in a satisfactory condition and appeared to go to sleep naturally. About three-quarters of an hour later she slept normally for forty minutes, and then she died suddenly in her sleep. The provisional diagnosis was coronary thrombosis.

POST-MORTEM FINDINGS (ABSTRACT ONLY)

Diagnosis : Acute heart failure, tumour of the left auricle, hyperpiesis.

There was no excess of pericardial fluid. Some hypertrophy of the left ventricle was present with well marked atheroma of the aorta; but the coronary vessels were excellent and the probe passed readily along them without finding any obstruction. No alteration in the size of any of the valve apertures was found, and all the valve cusps were thin and showed no evidence of previous infection.

When palpating the mitral valve a fairly firm tumour could be felt almost filling the left auricle. On approaching the left auricle from behind, this tumour could be more readily seen (Fig. 1). It was attached to the inter-auricular septum by a pedicle 23 mm. long and 16 mm. broad, the lower point of this pedicle being attached 8 mm. above the attachment of the mitral cusps. The tumour itself was roughly spherical, with a diameter of 40 mm. The length of the pedicle allowed the tumour to be pushed into the orifice of the mitral valve (Fig. 2) and also to fall over the openings of the pulmonary veins. In appearance the tumour was shiny, and there were many small polypi on the surface. It was white in colour save where hæmorrhage beneath the surface was shining through. It was peculiar in consistency, being somewhat rubbery or elastic. On section the tumour was yellow in colour and homogeneous, with several areas of recent hæmorrhage. There was no evidence of scarring



FIG. 1.—Posterior aspect of heart showing myxoma lying in the left auricle ; it is attached to the interauricular septum by a pedicle.

or contracture. (There was considerable shrinking on preservation, and this shows in the plate.)

The lungs showed congestion throughout, this being somewhat more marked at the bases, and there was considerable emphysema. The liver was slightly enlarged and was also congested. The kidneys were smaller than normal, with a very rough granular surface. On section there was increase of pelvic fat and decrease in the size of the cortical layer. The intercortical vessels stood out prominently.

Histological sections were prepared from the base of the tumour and from its free surface. These were stained by hæmatoxylin and eosin, by Van Gieson's stain, by mucicarmine, and by thionin. The tumour appeared lined by a single layer of endothelial cells under which was a thin layer of fibrous tissue. Immediately beneath this layer were masses of inflammatory cells and new



FIG. 2.—Photograph of heart before fixation, showing smooth and shiny tumour projecting through mitral orifice.

blood vessels or groups of endothelial cells which represented new capillaries awaiting canaliculization. Large masses of blood pigment were present, probably hæmosiderin, but little intercellular pigment could be found. Deeper within the section the tumour proper was found. This consisted of a finely fibrillar matrix, cells being relatively scanty. The matrix stained faintly blue with hæmatoxylin, but fairly deeply with mucicarmine and thionin. The cells were large with a vesicular nucleus, and in many cases they showed bipolar or unipolar projections.

Within the tumour proper groups of endothelial cells and capillaries with a single cell lining were found and blood pigment masses were still present, but were less marked. The myxoma cells tended to be arranged around these new blood vessels. The large areas of hæmorrhage were mainly confined to the sub-endocardial region, but deeply within the tumour there were small groups of free red cells. A small amount of elastic tissue was found throughout the sections examined. The picture was therefore one of a myxoma, the number of new blood vessels present hardly justifying the term angiomyxoma.

CLINICAL FEATURES

No one has yet reported the successful diagnosis of a primary innocent cardiac neoplasm during life. Pavlowsky (1919) made a diagnosis of primary sarcoma of the left auricle, but at the autopsy it was discovered that the tumour was on the right side. A primary malignant tumour, an invasive tumour of a sarcomatous type, was diagnosed by Shelburne (1935) in a case of a male aged 24 with a large blood-stained pericardial effusion.

In many of the reported cases, however, the diagnosis was suggested by



FIG. 3.—Section of cardiac myxoma ($\times 100$), showing fibrillar matrix and elongated cells.

certain points in the history, the physical signs, or in the reaction of the patient to treatment, and so it may be of interest to consider a few of the clinical pictures which have been described as follows.

(1) *Mitral Stenosis with Congestive Heart Failure.*

The picture of mitral stenosis with congestive heart failure is the commonest one to be described. A typical case is described by Jensen (1934) in a woman aged 32 who had complained of shortness of breath and œdema for two months,

and clinically showed ascites and a heart condition typical of mitral stenosis. There are three important points which appear, however.

- (a) The cardiac signs and especially the murmur vary from time to time. Thus in the case described by Bien and Ch'in (1936) a rough high-pitched systolic murmur present all over the præcordium, but loudest at the apex, was heard when the patient was in hospital but whilst an out-patient a rumbling mid-diastolic murmur or a third heart



FIG. 4.—Section of cardiac myxoma ($\times 450$), showing cells arranged near blood vessels; large amount of pigment.

sound prolonged into a diastolic murmur was found at the apex. Gilchrist and Miller point out that the obstruction of an auriculo-ventricular orifice by a tumour retards the blood flow and narrows the stream and this fictitiously produces the auscultatory signs of a valvular stenosis.

It is obvious that in certain positions the tumour will fall away from the valve orifice, with the result that the blood flow is not impeded and the heart sounds change in character.

- (b) These patients rarely give a previous history of antecedent diseases, such as rheumatic fever, chorea, growing pains or recurrent sore throats, which might have lead up to a mitral stenosis.
- (c) The history of cardiac debility is usually a short one.

(2) *Fainting Attacks and Loss of Consciousness with the Patient Erect*

The case described by Houck and Bennett (1929-1930) demonstrates well this group of cases. The patient was a female, aged 44, who had always enjoyed the best of health and denied all previous history of rheumatism. She was an athletic type and indulged in a considerable amount of swimming. Suddenly, six weeks before admission to hospital, she had a fainting attack as she stood up after leaving the water. After this, fainting attacks recurred at weekly intervals, always whilst the patient was erect. There followed in rapid succession dyspnoea with oedema of the ankles, cyanosis and orthopnoea. On admission to hospital, presystolic and systolic murmurs at the apex and a moderate degree of enlargement of the heart were found. She died suddenly in her sleep during the first night in hospital. At the autopsy a tumour was found in the left auricle which fitted snugly into the mitral orifice. It seems clear that in this group of cases the symptoms depend upon the tumour completely blocking the mitral orifice for a very short time whilst the patient is erect. They depend upon the tumour having a sufficiently long pedicle to allow some movement.

Another case of this kind is described by Gorlitzer (1934). Here a woman was admitted to hospital unconscious with twitching in all the extremities and with preserved reflexes. She had had several previous attacks of an "hysterical" type. At autopsy a myxoma of the left auricle was found with emboli in the left anterior cerebral artery, both middle cerebral arteries and the left posterior cerebral artery.

(3) *Sudden and Unexpected Death*

This group of cases really consists of the final stages of the ones previously described, although there is often no previous history of illness leading up to the final attack. Here the tumour probably does not fall back from the mitral orifice and death ensues. Lymburner's case (1934) was admitted to hospital for the treatment of septicæmia which was the result of a self-induced abortion, and she died suddenly. There were no abnormal clinical features found in the heart. In Houck and Bennett's case previously described and also in our case death took place quietly during sleep.

(4) *Relentless Progress of Heart Failure in spite of Adequate Rest and Digitilization*

We have already mentioned the case described by Bien and Ch'in, since it demonstrated the point of varying heart murmurs with the position of the

patient, and it is also an excellent example of this type of case. The patient was a male aged 59 when first admitted to hospital in 1934 complaining of shortness of breath which had been present for three weeks. During a stay in hospital of one month he made some improvement and was discharged on a maintenance dose of 0.1 g. of digitalis daily and was instructed to rest at home. This he did. During the following year the cardiac reserve became slowly reduced, so that from being able to walk two-thirds of a mile he could now walk less than a hundred steps, and in January 1935 signs of congestion were found and the patient was re-admitted to hospital. Thus although resting and receiving adequate digitalis and although he had been seen frequently at the cardiological clinic, the lesion first noted in January 1934 slowly progressed during the year until death took place in February 1935. This progress of symptoms is probably dependent upon the slow growth of the tumour; with more rapid onset or with more rapid retrogression of health dependent upon rapid increase in size such as would follow hæmorrhage into its substance.

(5) *Abnormal Radiological Shadows.*

The enlargement of the left auricle caused by the presence of a large tumour will sometimes produce alterations in the radiological contour of the heart. Bennett and Konigsberg (1938) describe a case, admitted to hospital with a pelvic abscess, who died whilst under an anæsthetic for its treatment. A skiagram showed a large bulge in the region of the pulmonary conus which was considered to be due to congenital abnormality. There was a myxoma in the left auricle. The tumour described by Gilchrist and Miller produced a projection into the posterior mediastinum together with marked enlargement of the heart both to the right and to the left.

(6) *Cardiac Irregularities*

Cardiac myxomas rarely produce irregularities of the pulse. This is readily understood, because as innocent tumours they do not interfere with the conducting mechanism. It is comparatively rare for even extensive involvement of the myocardium with secondary deposits from carcinoma or sarcoma to produce obvious changes in the electrocardiogram. Paroxysmal auricular tachycardia is described by Gilchrist and Miller in a male aged 57 who had complained of præcordial pain for two and a half months. These attacks of pain were brought on by lying flat in bed and were relieved by sitting up. At the height of an attack he "fell away in a trance." Each attack lasted from 10 to 15 minutes. The first diagnosis considered was an anxiety neurosis, but the presence of slight cyanosis and dyspnœa suggested an organic cause for the symptoms. The electrocardiogram showed short runs of auricular paroxysmal tachycardia and numerous auricular extrasystoles intermingling with normal rhythm. These attacks of paroxysmal tachycardia were reduced in

frequency under digitalis therapy, although whilst in hospital right-sided heart failure developed which did not respond to treatment.

(7) *Paroxysmal Dyspnœa*

If the tumour interferes with the orifices of the pulmonary veins instead of with the mitral orifice it will cause sudden back pressure in the pulmonary circulation and thus give rise to pulmonary œdema and dyspnœa. It has frequently been noted that in cases of heart failure due to the presence of a tumour in the left auricle the breathlessness is out of all proportion to the degree of decompensation. Bien and Ch'in say that their patient was suddenly awakened at midnight with a sense of suffocation and had profuse perspiration and palpitations only relieved by expectorating large quantities of frothy sputum. Gilchrist and Miller also describe attacks of paroxysmal nocturnal dyspnœa. Ernstene and Lawrence (1936) report a case, not of myxoma but of an occluding thrombus in the left auricle, in which for several months there had been paroxysms of breathlessness which caused the patient to sit up in bed, when he promptly lost consciousness. Each attack lasted for less than fifteen minutes.

After considering the groups of cases described above, we would suggest that no particular symptom or sign can be taken as diagnostic of an intracavitary tumour of the heart, save perhaps the rare abnormal skiagram; but that, if in any patient the history, the physical signs, and the subjective symptoms do not readily fall together into a complete picture, then the presence of such a tumour should be considered. The case can then be reassessed with this diagnosis in view. Especially might this be true in cases of mitral stenosis who strongly deny all antecedent illness and in whom the cardiac disability is an exceedingly short one.

PATHOLOGY

Although at least 100 descriptions of cardiac myxomas have been published the majority of reported cases are not accepted by all pathologists. Writing in 1922 Husten said that, of the 71 reported cases he discussed, only 9 were true myxomas, all the others being thrombi. On the other hand Ribbert (1924) disagrees with this view and considers that the majority at least of the reported cases are true tumours. Bacaloglu *et al.* (1933), call these tumours "thrombus myxoides" and say that "les myxomes du cœur sont à l'envers de la conception classique des tumeurs des plus rares," and Clerc *et al.* (1937) say that between the true myxomatous or myxosarcomatous tumours and organized thrombi all intermediate forms are possible.

The possible origin of these tumours may be listed :

- (1) They are true myxomatous tumours arising, as Ribbert suggests, from myxomatous rests in the region of the fossa ovalis in the interauricular septum.
- (2) They are thrombi undergoing myxomatous degeneration.

- (3) They are œdematous thrombi, the matrix not being true myxomatous tissue but fibrin swollen by œdema fluid.
- (4) They represent myxomatous degeneration in a fibroma.

The main argument lies, it seems to us, between the first two of these possible origins. Are these true tumours or are they thrombi undergoing myxomatous degeneration? The present view seems to be that they are true tumours. Thus Yater (1931) says: "It seems to me that the argument concerning the nature of these myxomatous masses is all in favour of their neoplastic origin," and Ewing (1928) says "Whilst many of the larger tumours may be difficult to identify it seems unlikely that a simple organizing blood clot can reproduce the positive features of the true myxomas. Hence the great majority of the reported cases of cardiac myxoma are probably genuine."

The presence of small myxomas on the heart valves is not disputed, and cases have been reported by Jaleski (1934) and by Abrahamer (1931), but the origin of the large masses found in the auricle more often on the left than on the right is a debated question. The arguments in favour of these masses being true neoplasms are

(1) Myxomas are always found in the auricles, whereas thrombi are more common in the ventricles. They arise near the fossa ovalis where it is known that myxomatous rests may occur.

(2) There is no previous history in the majority of cases which would lead to stasis in the heart chambers and so allow thrombi to form. Samuel Wilks (1889) very beautifully describes the formation of *antemortem* thrombi or "polypi" in the dilated chambers of the heart due to the stagnation of blood in the recesses of the columnæ, especially in the left ventricle and the right auricle. He stresses that there must be stagnation to allow thrombus formation.

(3) Myxomas are uniform throughout except where there is hæmorrhage; there is no evidence of the lamination found in the more common *antemortem* thrombus.

(4) Microscopically, myxoma shows a poverty of cells, but those present are characteristically spindle or star shaped cells with processes anastomosing or disappearing into the matrix. They may be scattered throughout the tumour or be arranged round the blood vessels or underneath the capsule if the tumour shows peripheral growth. The characteristic cells will not, of course, be found in a thrombus. Elastic tissue may be found in either case. The blood vessels of a tumour are arranged in a uniform manner throughout the neoplasm, and in a thrombus they tend to be scanty deep within the mass.

(5) A thrombus tends to retract and will show scarring, whilst a neoplasm may be smooth, villous, papillomatous or polypoid.

(6) Chemically the presence of mucin cannot be used as an argument either way, since mucin may be found in an undoubted thrombus. The blood pigment in a myxoma is hæmosiderin throughout, whereas in a thrombus the peripheral

pigment is hæmosiderin and the pigment at the centre is the iron-free hæmatoidin.

It is unlikely that these neoplasms are fibromas undergoing myxomatous degeneration because :

(1) They are the commonest primary tumour of the heart, whereas Yater says that only 25 cases of fibroma had been reported up to 1931. The fibromas are never larger than a cherry and in the majority of cases they were placed on the heart valves.

(2) Myxomatous degeneration in an innocent tumour is usually looked upon as a prelude to malignant change and myxosarcomas are exceedingly rare. If all myxomas were an intermediate stage between an innocent neoplasm and a malignant one we should expect obvious primary malignant tumours of the heart to be more frequent than they appear to be in the literature.

Our case answers as far as possible the criteria laid down for the diagnosis of a cardiac myxoma. The tumour was totally unlike any thrombus we have ever seen in a heart, and we believe it to be a true neoplasm.

SUMMARY

(1) The clinical features and postmortem findings in a case of cardiac myxoma are described.

(2) The symptoms and signs in reported cases of cardiac myxoma are reviewed. Obstruction of the mitral orifice by the tumour may produce murmurs like those of mitral stenosis, or may cause fainting attacks related to posture or sudden and unexpected death. Obstruction of the pulmonary veins may cause paroxysmal dyspnoea.

(3) The pathology of cardiac myxoma is discussed and the various views as to their origin are mentioned. Reasons are given for regarding them as true myxomatous tumours rather than as thrombi or fibromas which have degenerated.

We wish to thank Dr. E. C. Hadley, Medical Superintendent of the City General Hospital, Leicester, for his permission to publish this case and the Librarians of the Royal Society of Medicine and the British Medical Association for much help with the bibliography.

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STANDARDIZATION OF METHODS OF MEASURING THE ARTERIAL BLOOD PRESSURE

A JOINT REPORT OF THE COMMITTEES APPOINTED BY THE
CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND AND THE
AMERICAN HEART ASSOCIATION.

EDITORIAL

The genesis of the joint report that follows may be explained shortly. In September 1938 the American Heart Association appointed a committee to draw up recommendations for a standard technique for taking arterial blood pressure, and asked the Cardiac Society of Great Britain and Ireland if they would like to appoint a similar committee, which should if possible issue a joint report with the American Committee. The Council of the Cardiac Society approved of this course and appointed a Committee for the purpose.

The reader may feel that such recommendations are not needed and that everyone knows how to take the blood pressure and does it in the same way. The committee have learnt that this is not the case and that many physicians differ in small points of technique, often without realizing that their custom is not universally accepted.

The British Committee met on November 19 and had before them the results of various preliminary enquiries and the excellent short recommendations put forward by a committee of the Assurance Medical Society in May 1931 and published in their journal. The British Committee drew up some recommendations which were discussed with many members of the Council and with other physicians and physiologists. At a second meeting on January 21, 1939, these were put into final shape and were sent to America early in February.

The recommendations and report of the American committee were received about this time, and it was obvious there was a good deal of common ground, but a few outstanding differences. A composite report was drawn up incorporating these agreements and differences, and this has since been the basis for discussion in both countries. This was then brought before the Council of the Cardiac Society, who authorized their committee to publish an agreed draft within the compass of these recommendations.

The British and American committees have both accepted many suggestions where they thought the other had made useful additions or had expressed the

recommendations more clearly ; both, however, have retained to some extent their own phraseology where they thought this more appropriate to their country and have set forth with different emphasis the three remaining points in which agreement was not reached. Two of these three are simple—the British committee expressing a preference for the mercurial manometer as less likely to get out of order, and expressing no choice as to whether the patient is lying down or sitting provided he is comfortable ; the American committee preferring that he should be seated, but expressing no preference between the mercurial and aneroid instruments, provided they are in good condition.

The third more important difference is in the method of recording the diastolic pressure. Both committees agree that the point where the loud, clear sounds change abruptly to the dull and muffled sounds should be recorded. The British committee think this is the only point that should be recorded and that it can nearly always be detected accurately, though at times only with difficulty. The American committee, influenced perhaps by this difficulty, recommend that the point where the sounds disappear should also be recorded.

Apart from these three differences, which are dealt with in the report, and the phraseology, the reports and recommendations were in substantial agreement, and it has been agreed, therefore, that they should be published in each country over the joint signatures of both committees.

MEMBERS OF THE COMMITTEE FOR THE STANDARDIZATION OF BLOOD PRESSURE READINGS

APPOINTED BY THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

Dr. Crichton Bramwell, Manchester, England
Dr. Maurice Campbell, London, England
Dr. T. F. Cotton, London, England
Dr. William Evans, London, England
Dr. A. R. Gilchrist, Edinburgh, Scotland
Dr. John Hay, Liverpool, England.

APPOINTED BY THE AMERICAN HEART ASSOCIATION

Dr. M. H. Barker, Chicago, Illinois
Dr. Joseph Erlanger, St. Louis, Missouri
Dr. Jonathan Meakins, Montreal, Canada
Dr. Ralph Schneider, New York City
Dr. S. B. Scholz, Jr., Philadelphia, Pa.
Dr. Harry Ungerleider, New York City
Dr. Paul White, Boston, Mass.
Dr. Carl Wiggers, Cleveland, Ohio
Dr. Irving Wright, New York City, Chairman.

JOINT REPORT ON THE METHOD OF MEASURING ARTERIAL BLOOD PRESSURE

INTRODUCTION

It has long been realized by many teachers and practitioners of medicine that the wide variations in blood pressure records of a single subject were due not only to changes in the pressure from time to time under different conditions, but also to the different methods used by the observers. The interpretation of the sounds heard on auscultation is an important cause of divergent readings. A recent survey of Wright and others (*American Heart Journal*, 16, 469, 1938) revealed a serious lack of agreement as to the correct technique for taking and interpreting the blood pressure. Similar uncertainty was found among insurance companies as to what they should require of their examiners in this regard. Experiments with multi-aural stethoscopes showed that recent years have brought little if any improvement, as the discrepancy among the recently qualified was as great as among their seniors.

The Committees for the standardization of methods of measuring arterial blood pressure appointed by the American Heart Association and by the Cardiac Society of Great Britain and Ireland have tried to bring about a crystallization of the best available thought on this subject. If feasible, the Committees were asked to make joint recommendations which might be accepted as a standard for practising physicians, medical teachers, and insurance companies.

After a careful study of the material available from many sources and after much discussion the Committees jointly recommend the following procedure as the standard method for taking and recording blood pressure readings in man. Some of these recommendations are dealt with in more detail in the explanatory notes. The British and American Committees have decided to publish over their joint signatures reports which differ slightly in wording and phraseology. In the few instances where there was any difference of opinion, the views of both Committees have been included in each report.

RECOMMENDATIONS

1. *The instrument*

The equipment to be used for measuring arterial blood pressure, whether of the mercurial or of the aneroid type, must be in good condition and requires to be calibrated at frequent intervals against a standard mercurial manometer. The British Committee think that the mercurial type is the most dependable. The proper care of these instruments and the importance of a standard armlet are dealt with in the explanatory notes that follow.

2. *Position of the patient*

The patient should be allowed time to recover from any recent exercise or excitement. He must be comfortable and may be either lying or sitting. The American Committee recommend that he should be sitting and that, if not, a special note should be made.

The arm, relaxed and comfortably supported at the patient's side, must be laid bare to the shoulder to avoid any constriction by a rolled up sleeve and to facilitate proper application of the armlet.

3. *Application of the cuff*

The cuff must be of standard size, with a rubber bag at least 12 cm. wide. The cuff, completely deflated, should be applied with the middle of the rubber bag over the inner side of the arm, and its lower edge one inch above the bend of the elbow. It should fit closely and evenly round the arm to ensure against bulging at the sides when it is inflated.

4. *Determination of the systolic pressure by palpation*

A preliminary approximate reading of the systolic pressure should be taken by palpation as a check on auscultation; the pressure in the armlet should be raised quickly in steps of 10 mm. until the radial pulse ceases, and then allowed to fall rapidly.

5. *The application of the stethoscope*

The brachial artery should be located by palpation, and the stethoscope applied lightly and accurately over it, just below but not in contact with the cuff. The hand may be pronated or supinated according to the position yielding the stronger brachial pulse.

6. *Determination of the systolic pressure by auscultation*

After inflating the cuff quickly to a pressure about 30 mm. above the level of the systolic pressure as found by palpation, auscultation should be conducted during slow deflation.

The systolic pressure is the highest level at which successive sounds are heard.

7. *Determination of the diastolic pressure*

With the pressure continuing to fall slowly and uniformly, the sound increases to its maximum intensity and then decreases, at first gradually and later suddenly, and soon disappears. The point where the loud clear sounds change abruptly to the dull and muffled sounds should be taken as the diastolic pressure.

The American Committee recommend that if there is a difference between this point and the level at which the sounds disappear completely the latter reading should be regarded also as a measure of the diastolic pressure. This should then be recorded in the following form—Rt (or Lt) 140/80-70 or 140/40-0, or if these two levels are identical as 140/70-70. The British Committee disagree with this recommendation and think that except in aortic regurgitation it is nearly always possible to decide the point at which the change comes and that this is the only reading that should be recorded.

EXPLANATORY NOTES

The Committees feel that certain other considerations in addition to these specific recommendations should be taken into account, and for convenience they are numbered in the same way as the relevant recommendations.

1. The instrument

Frequent discussions have taken place as to relative merits of various types of blood pressure apparatus. The mercury manometer and the aneroid type of apparatus are both capable of correct readings if in good condition, and both may be inaccurate if they are not. This is sometimes neglected in reference to the mercury manometer, which should be tested at intervals in the following ways :

- (a) The level of the mercury at rest should be at the zero mark. If any mercury has leaked out it must be replaced.
- (b) If the small air vent at the top of the glass tubing becomes clogged there may be a lag which will give false readings.
- (c) The blood pressure box must be on a level surface, since tilting of the manometer will lead to mistakes ; it should also be level with the observer's eye.

The aneroid type of instrument, if used, must be calibrated frequently against a mercurial manometer. The needle should stand at zero when the rubber tubing is deflated, and move immediately when inflation begins. A stop pin at the zero mark makes it difficult to check its accuracy.

In both types of instrument the valve must be competent. The entire system, including the rubber tubing and bag, must be free from leakage.

The rubber cuff must be at least 12 cm. wide ; it must be 23 cm. long and its covering must be of inextensible material and, if not of leather or made rigid with metal ribbing, should extend as a band 15 cm. wide for a distance of 60 cm. beyond the edge of the rubber cuff and then taper gradually to an apex during a further length of 30 cm. If bulging occurs the reading may not be accurate.

For children the rubber cuff may be narrower and the covering shorter.

New types of cuffs, using a zipper mechanism or rubber hooks on a ribbed extension the same width as the cuff, may prove to be more satisfactory than the long tapering cuff end.

2. The patient

The sitting position was selected by the American Committee because for practical purposes it simplified the taking of large numbers of blood pressure readings. The British Committee did not think there was any significant difference between the readings obtained in the sitting and lying positions.

Certain physical and psychological factors should be considered. Enquiry should be made as to the patient's activity just before the examination, as strenuous exercise may produce changes in the figures recorded. Blood pressure observations taken immediately after meals differ from those taken before

meals. There are physiological variations in the level of the blood pressure, so that for research purposes observations should be made with the same relationship to meals, sleep, exercise, and allied factors.

A rest period of from 10 to 15 minutes before taking blood pressure readings would eliminate or minimize certain of these factors. Tachycardia in itself sometimes causes a raised systolic pressure. Appreciation of the stress or anxiety through which the patient is passing is important to the examiner. Any appearance of concern on his part may unduly alarm the patient, thereby increasing the pressure. Apart from this, the first reading is often much too high because of the patient's nervousness.

3. *Application of the cuff*

Venous congestion must be avoided as far as possible ; there should be no constricting bands on the patient's arm and the pressure cuff should not be kept inflated longer than is necessary to take the reading ; it must be deflated completely before any further determinations are made. In obese subjects special care in the application of the cuff is necessary to prevent bulging. Deflation should be at the rate of about 3 mm. of mercury per second.

4. *The systolic blood pressure*

If the method of palpation is used before the auscultatory method as recommended, the unusual case with a silent gap will not be missed. In these cases after the first sounds have been heard there is an auscultatory gap below which the sounds reappear. This silent gap is not very uncommon in cases of aortic disease and hypertension

8. *Cardiac arrhythmias and aortic valvular disease*

The determination of blood pressure in these conditions is more difficult and the following recommendations are made :—

- (a) Where there are extrasystoles the higher pressure of the beat that follows should be ignored.
- (b) In auricular fibrillation only approximate blood pressure readings can be obtained ; the systolic value should be taken at the point where the majority of beats appear, and the diastolic (if at all) at the point where they become dull and muffled. The American Committee suggest that the average of a series of such readings should be noted as the systolic and diastolic pressures.
- (c) Alternation in the strength of the beats (*Pulsus alternans*) must be looked for carefully. It must be distinguished from the alternating values produced by regular alternate extrasystoles (*Pulsus bigeminus*).
- (d) In aortic stenosis with a slow rising or anacrotic type of pulse, auscultation may give a false systolic reading and palpation may be more accurate ; often a satisfactory diastolic reading cannot be obtained.
- (e) In aortic regurgitation with a collapsing pulse the diastolic and point is marked by a less obvious change in the quality of the sounds, which may be difficult to appreciate.

9. General

In speaking of the changes which the sounds undergo, the term *points* is suggested for use instead of the commonly used term *phase*, since the latter implies a period of time, whereas the *points* are in fact the precise moments at which one phase changes into the next.

The use of a single figure for a pressure that varies so rapidly cannot be accurate to within from 5 to 10 mm. of mercury. For special accuracy several determinations should be made and the highest and lowest should be recorded.

If the pulse feels different on the two sides the blood pressure should be taken in both arms.

In the presence of unexplained high pressure in the arm it should be taken in the leg also, so that coarctation of the aorta may be detected.

A special cuff is necessary to record the blood pressure easily and accurately in the leg. The rubber bag should be 15 cm. wide and its covering should be 17 cm. wide and 30 cm. longer than in the case of the armlet. The patient should be in the prone position with the leg extended and the sounds should be auscultated over the popliteal artery.

In detailed researches on blood pressure the use of a basal pressure might be considered, after preparation similar to that used for basal metabolism. It should be determined 10-12 hours after the last meal of the previous night, and after resting half an hour in a warmed room. Difficulties in the use of this procedure in practice are obvious, and observations suggest that after 15 minutes the pressure has generally fallen to a basal level.

A defect of hearing in the examiner may call for the use of a stethoscope with some form of amplifier.

It is hoped that a critical attitude towards this subject on the part of physicians generally will result from the efforts of these Committees, so that every precaution will be taken to obtain conscientious and unbiased records through the use of the standard technique suggested here. These recommendations are not intended to discourage other methods of observation when indicated in special situations.

THE EFFECT OF POTASSIUM ON THE HEART IN MAN

BY

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It is just one hundred years since Blake (1839) reported his "observations on the physiological effects of various agents introduced into the circulation." Among these were various salts of potassium, and he showed that when potassium carbonate, for instance, in doses of fifteen grains dissolved in six drachms of water was injected into the jugular vein in dogs, the animal was dead in forty-five seconds. He concluded that the action was a direct one upon the heart and that it was not harmful in therapeutic doses on account of the speed with which it was excreted by the kidneys.

During the intervening century it has been left to the physiologists to investigate the action of potassium salts upon the heart, work which has naturally been carried out upon the experimental animal. So far as the clinician was concerned, potassium, originally in the form of the citrate and the acetate and later as the chloride, rapidly came into favour as a diuretic, and, while there was a general feeling that in excess these salts might have their disadvantages, few, if any, experiments were carried out in man. Smillie in 1915 reported five cases of chronic nephritis to whom he had given 5 or 10 grammes of potassium chloride, and in one of these there was a sudden attack of intense cyanosis and prostration, preceded by præcordial pain, from which the patient took a fortnight to recover. From his work on potassium chloride as a diuretic, Blum (1920) recommended extreme caution in its use in patients with cardiovascular disease. Magnus-Levy (1920) also reported toxic effects from the use of potassium salts in a few patients with heart disease, and Webster (1927) stated that potassium salts by mouth "may cause irregularity of the heart and aggravation of symptoms of already existing renal or heart disease."

METHODS OF PRESENT INVESTIGATION

As the result of the observation of certain changes in the electrocardiograms from patients that were receiving potassium salts, it was decided to carry out a more careful study of the effects of such salts upon the heart in man, not only to gain some information as to possible dangers in their therapeutic applica-

tion, but also in an attempt to throw some light on their function in the aetiology of certain disorders of the heart.

The effect of potassium salts upon the heart has been studied in 24 patients, including the 5 already reported upon elsewhere (Thomson 1939); in addition the serum potassium and its alterations under certain conditions have been studied in a further 11 patients with heart disease. For the purpose of this paper, however, only the first 24 will be considered. This group included twelve patients with hypertension, two of whom had diabetes mellitus and one slight thyrotoxicosis; five with advanced chronic nephritis; two with mitral stenosis and normal rhythm; one with coarctation of the aorta; one with luetic aortic incompetence; one with thyrotoxicosis; one with the "menopausal syndrome"; and one with allergy.

Potassium was given by mouth in the form of the citrate and the chloride, the usual dosage in the case of both salts being 5 grammes thrice daily at 8.30 a.m., 1.30 p.m., and 7 p.m., but several patients were given smaller amounts. Blood for the estimation of the serum cations was taken at noon, the patient having had nothing to eat since breakfast at eight; it was obtained from the antecubital vein without the use of stasis and the serum was separated one and a half hours later.

Electrocardiograms were practically all taken at the same time of day—shortly before the midday meal—with the patient in bed, and every care was taken to ensure that the standardization was uniform, i.e. 3 millivolts=3 cm. displacement of the fibre. In all instances they were taken both before and during the administration of potassium, and generally at least one was taken a week after it had been stopped.

The serum cations were estimated by the following methods; potassium, Kramer and Tisdall (1921) as modified by Peters and Van Slyke (1932); sodium, Butler and Tuthill (1931); calcium, Kramer and Tisdall (1921) as modified by Clark and Collip (1925). The urease method was used for the estimation of the blood urea, and the hæmoglobin was estimated by means of the Haldane hæmoglobinometer, the blood always being taken from the ear without stasis at the same time of day.

RESULTS : (A) POTASSIUM AND THE T WAVE

Potassium salts were administered to 24 patients; changes in the T wave were observed in 15, but they were either absent or insignificant in 9. The 15 that showed such changes were 5 with hypertension, 5 with chronic nephritis, and 5 others; details are given in Table I.

The change in the T wave consisted of an increase in the height of the wave in 14 cases. This increase in height occurred in different leads, in one lead only or in all three, and in practically every case disappeared after potassium was stopped. Fig. 1 shows a typical example of the change obtained. In the fifteenth case the changes in the T wave were quite different in type, as can be seen from Fig. 2 (see page 273).

TABLE I

INCREASE OF THE HEIGHT OF THE T WAVE IN THE ELECTROCARDIOGRAM WITH INCREASE IN THE SERUM POTASSIUM

Case Number	Diagnosis	Serum Potassium in mg. per 100 c.c.		Electrocardiographic Changes in the Height of the T Waves
		Before Administration of Potassium	During Administration of Potassium	
7	Malignant Hypertension	11.9	18.9	Increase
3	Malignant Hypertension	10.1	22.9	Increase
1	Essential Hypertension	17.2	21.8	Increase
8	Essential Hypertension	19.6	21.5	Increase
2	Essential Hypertension	15.5	21.2	Increase
4	Chronic Nephritis ..	20.5	31.6	Increase
5	Chronic Nephritis ..	17.0	32.8	Increase
9	Chronic Nephritis ..	22.1	25.1	Increase
10	Chronic Nephritis ..	20.7	33.1	Increase
22	Chronic Nephritis ..	22.6	—	Increase
11	Mitral Stenosis ..	19.1	28.9	Increase
12	Aortic Incompetence ..	17.8	31.8	Increase
6	Thyrotoxicosis ..	16.1	23.0	Increase
23	Menopausal Syndrome..	16.4	—	Increase
13	Allergy ..	19.4	21.7	Increase
14	Malignant Hypertension	15.1	22.2	No Increase
24	Essential Hypertension..	15.3	—	No Increase
15	Essential Hypertension ; Diabetes Mellitus ..	19.7	21.6	No Increase
16	Essential Hypertension ; Diabetes Mellitus ..	15.1	18.1	No Increase
17	Essential Hypertension ; Thyrotoxicosis ..	19.1	25.3	No Increase
18	Essential Hypertension ..	18.8	20.4	No Increase
19	Essential Hypertension ..	17.0	16.7	No Increase
20	Coarctation of Aorta ..	16.2	17.3	No Increase
21	Mitral Stenosis ..	15.6	15.7	No Increase

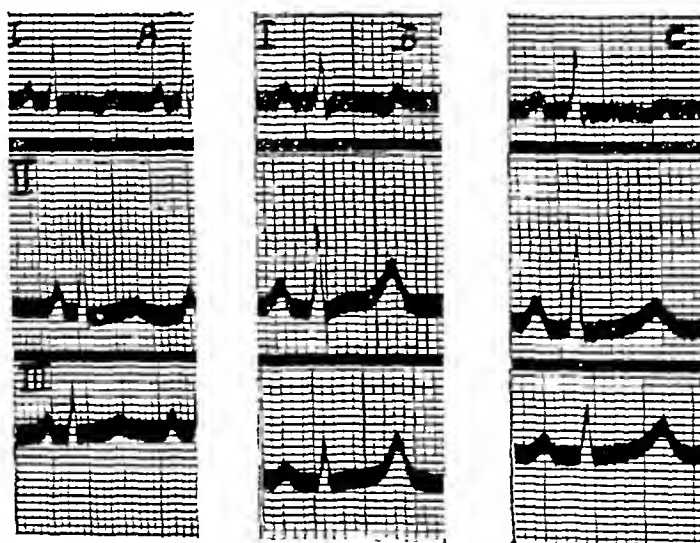


FIG. 1.—Electrocardiograms from case 4, with chronic nephritis.

(A) Before administration of potassium salts.

(B) After 71 g. of potassium chloride given during 7 days, showing heightened T waves in all leads (serum potassium increased from 20.5 to 31.6 mg. per 100 c.c.).

(C) After 14 days without any potassium salts, showing T waves diminished in height (serum potassium 21.4 mg. per 100 c.c.).

In Table II the findings in six of these patients have been given in more detail. The increase in the height of T varied considerably, from 1 to 4 mm., and in some cases it was more than doubled in height. This alteration in the height of the T wave could not be correlated with any change in the rate of the heart, in the height or width of QRS, or in the length of the S-T segment.

TABLE II
MORE DETAILED EFFECTS OF THE ADMINISTRATION OF POTASSIUM IN SIX CASES

Number of Days from Start	Serum Potassium	Serum Sodium	Serum Calcium	Blood Urea	Haemoglobin per cent.	Height of T Wave in EC. in mm.			Dosage of Potassium Salts
	in mg. per 100 c.c.					T _I	T _{II}	T _{III}	
Case 1. Essential Hypertension									
0	17.2	323	10.2	31	102	2.0	2.0	-0.5	Days 0-14, pot. cit. 15 g. daily.
7	18.3	324	9.5	26	112	2.0	2.0	-0.5	
14	21.3	313	10.0	26	110	3.0	3.0	-1.0	Days 7-14, pot. chlor. 15g. daily.
21	21.8	325	10.7	24	88	4.5	2.0	-1.5	
28	16.5	324	10.5	24	102	2.0	1.5	-0.5	
Case 2. Essential Hypertension									
0	15.5	328	11.4	23	110	3.0	2.5	-0.5	Days 0-14, pot. cit. 15 g. daily.
7	18.5	325	—	28	112	6.5	3.5	-2.0	
14	21.2	333	11.0	27	108	5.0	4.5	-0.5	Days 7-14, pot. chlor. 15 g. daily.
21	15.3	326	10.7	21	102	2.0	2.0	-0.5	
Case 3. Malignant Hypertension									
0	10.1	310	10.3	16	86	-0.5	D*	2.0	Days 0-12, pot. cit. 15g. daily.
7	11.8	311	10.5	22	82	0.0	D	1.5	
12	22.9	306	11.2	33	98	1.5	4.0	2.5	Days 7-12, pot. chlor. 15 g. daily.
24	7.5	307	10.3	20	84	-2.0	D	1.5	
Case 4. Chronic Nephritis									
0	—	—	—	—	—	D	1.0	1.0	Days 5-12, pot. cit. 71 g.
2	20.5	—	9.3	143	65	—	—	—	
12	31.6	—	11.0	148	56	D	5.0	5.0	—
26	21.3	—	9.6	180	55	D	3.0	3.5	
Case 5. Chronic Nephritis									
0	17.0	—	9.6	62	96	-2.0	-1.5	0.5	Days 1-8, pot. cit. 15 g. daily.
8	32.8	—	9.9	70	92	1.0	2.0	1.5	
15	16.0	—	9.6	81	82	1.0	-0.5	-1.5	Days 6-8, pot. chlor. 15 g. daily.
Case 6. Thyrotoxicosis									
0	16.1	—	10.8	30	92	1.0	1.5	1.0	Days 0-6, pot. cit. 145 g.
11	23.0	—	10.8	44	102	2.0	4.0	1.0	
21	19.4	—	9.9	26	105	1.5	2.0	1.5	Days 7-11, pot. cit. 15g. daily, pot. chlor. 15g. daily.

* D=Diphasic.

The amount of potassium salts ingested before this change was produced varied considerably. In one patient it occurred after only 20 g. of the citrate given during four days. In others, 210 g. of the citrate and 105 g. of the chloride given over a period of two weeks did not produce it. Of the 15 patients who showed changes in the T wave, 7 received the citrate alone, 7 received both citrate and chloride simultaneously and 1 received only the chloride, while of the 9 who showed no such change, 7 received the citrate alone and 2 received both salts.

The concentration of serum potassium at which this change occurred was most inconstant, a more constant figure being the increase in its level. As can be seen from Table I, in thirteen of the patients who showed a change in the T wave, and in whom figures are available for the serum potassium both before and during the administration of potassium salts, the rise in the serum potassium varied from 1.9 to 15.8 mg. per 100 c.c., the average being 8.3 mg., while the comparable figures for the patients with no change in the T wave were -0.3 to 7.1 mg. per 100 c.c., giving an average of 2.6 mg. In only one instance did the serum potassium fail to return to practically the original level, and in this case the T wave also failed to return to its original height.

This heightening of the T wave was accompanied by a slight or moderate elevation of the S-T segment in a few of the patients (Fig. 1), and inversion occurred in one case (Fig. 2).

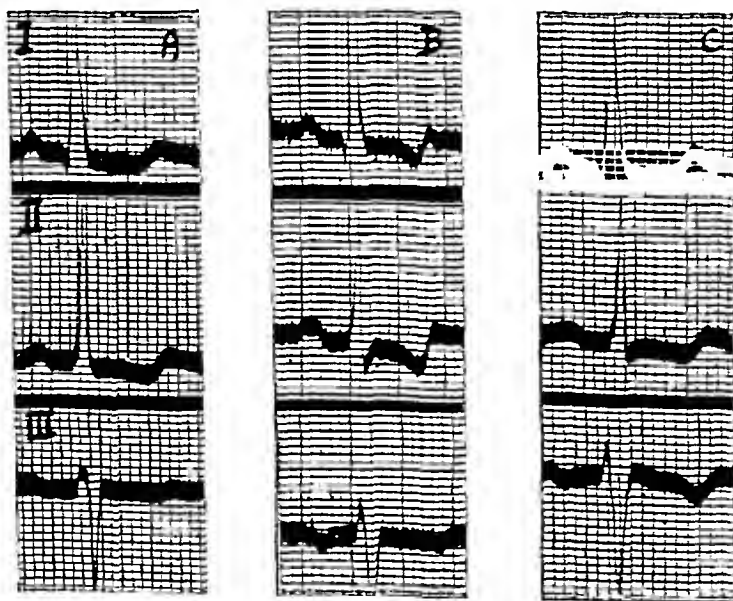


FIG. 2.—Electrocardiograms from Case 12, with luetic aortic incompetence.

(A) Before administration of potassium salts.

(B) After 192 g. of potassium citrate given during 14 days, showing T waves increasingly diphasic in all leads (serum potassium increased from 17.8 to 31.8 mg. per 100 c.c.).

(C) After 7 days without any potassium salts, when the T waves were almost, and the serum potassium was quite, back to the original levels.

No constant change was found in any instance in the levels of the serum sodium or calcium or the blood urea.

(B) POTASSIUM AND CONDUCTION

In two patients the administration of potassium salts was accompanied by impairment of conduction, and, in view of the importance of these observations, it is proposed to describe them in detail.

Case 23. A woman, aged 45, gave a three years' history of short attacks of palpitation, which began and ended gradually. She had lost weight, and had some symptoms suggestive of thyrotoxicosis, but on examination no evidence of this could be found and the basal metabolic rate was only +12 per cent. The blood pressure was 145/90 mm., the pulse was 96, and regular, the heart was not enlarged, and the heart sounds were pure and clear. A diagnosis of the menopausal syndrome was made. Serum potassium was 16.4 mg.; serum calcium, 11.9 mg.; blood urea 20 mg., in each case, per 100 c.c.

Potassium chloride was given in doses of 5 g. thrice daily, combined after one day with the same amount of potassium citrate. During the second night

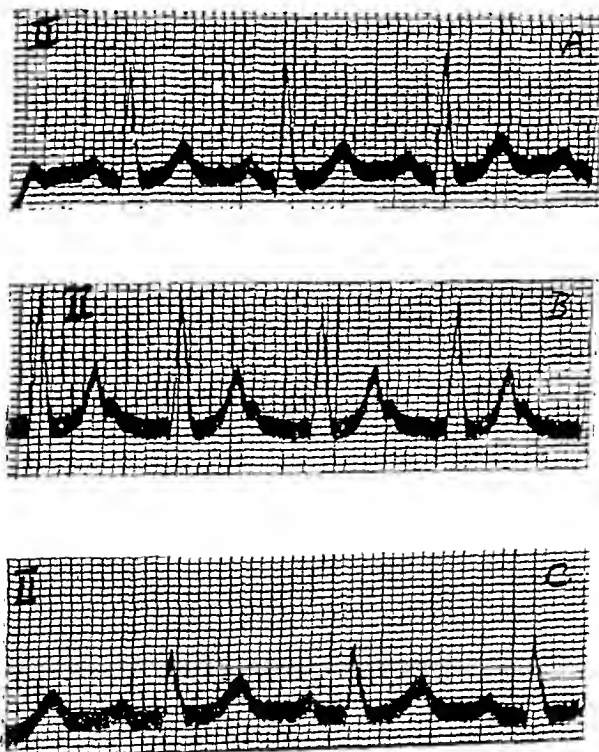


FIG. 3.—Electrocardiograms in Case 23.

- (A) Showing the P-R interval within normal limits.
- (B) Three days later, after the patient had received 40 g. of potassium chloride and 15 g. of potassium citrate, showing lengthening of P-R interval and heightened T wave.
- (C) Seven days from the start, when no potassium salts had been given for three days, showing the P-R interval again within normal limits and the T wave back to its original height.

of potassium administration, after she had received 35 g. of the chloride and 10 g. of the citrate, she complained of a heavy feeling in the legs, and the pulse was found to be 120 per minute and regular. Next day, three hours after another 5 g. each of the chloride and the citrate, there was prolongation of the P-R interval and heightening of the T wave (Fig. 3 B). Potassium salts were stopped on the fourth day, when the patient felt very hot and flushed and complained of a sinking feeling, nausea, and a tingling sensation in the arms, but not of palpitation.

Three days later the P-R interval had become normal (Fig. 3 C) and remained so in a subsequent record.

Case 11. A woman, aged 46, was admitted on account of increasing dyspnoea on exertion and cough; during the last three months orthopnoea and swelling of the ankles had developed.

On examination she was found to be a typical case of mitral stenosis with normal rhythm and signs of early congestive heart failure.

The serum potassium was 20.6 mg.; serum calcium, 10.1 mg.; and the blood urea 39 mg., in each case, per 100 c.c. Hæmoglobin, 100 per cent.

After a week in hospital, the administration of potassium chloride was started in doses of 5 g. thrice daily. Two hours after the fourth dose she felt cold and sick and complained of a sensation of tingling everywhere and of sinking through the bed; the pulse was 112 per minute and regular. An hour later, while still regular, it had fallen to 40, rising two hours later to 60 per minute and still regular. On the following day, that is after the patient had taken 30 g. of potassium chloride in all, it was stopped on account of vomiting and evacuation of the bowels, the pulse being 42 per minute and regular.

Eight days later, the serum potassium being 19 mg. per 100 c.c., administration of potassium salts was begun again, and during the next sixteen days 125 g. of potassium citrate was given without the production of any toxic effects. On the seventeenth day potassium chloride, in doses of 3 g. thrice daily, was combined with the citrate which was now being given in doses of 5 g. thrice daily, and the following day, twenty-five minutes after her second dose of each of these salts, she complained of feeling queer and the pulse was found to be 72 per minute and regular. Fifty minutes later it was 30 and regular, the patient complaining of no discomfort; and after another thirty minutes the pulse was 44, while an hour later it was 56 per minute and regular.

In view of these signs of toxicity, it was decided to follow the course of their development more carefully by giving the patient a dose of the two salts and following the effect on the heart by means of the electrocardiograph and by recording the rate of the heart at the apex every minute. Accordingly, the next day, after a control electrocardiogram showing normal sinus rhythm (Fig. 4 A), a sample of blood was obtained which gave the following results, serum potassium, 19.1 mg.; serum calcium, 11.6 mg.; blood urea, 30 mg., in each case, per 100 c.c. The patient was then given 5 g. of potassium chloride and 5 g. of potassium citrate by mouth. Thirty minutes later there was some increase in the height of the T wave. Forty-three minutes after the ingestion of the potassium salts, the ventricular rate suddenly slowed and became irregular,

and there were two periods of cardiac asystole and slight prolongation of the P-R interval (Fig. 4 B). (It should be noted that T III was negative in the control). Venu-puncture was performed as soon as this electrocardiogram was taken and the serum potassium was 28.9 mg. ; serum calcium, 11.5 mg. ; and the blood urea, 34 mg., in each case, per 100 c.c.; the patient complained of feeling faint, but objectively the only change noted was deepening of the respirations and some pallor of the face.

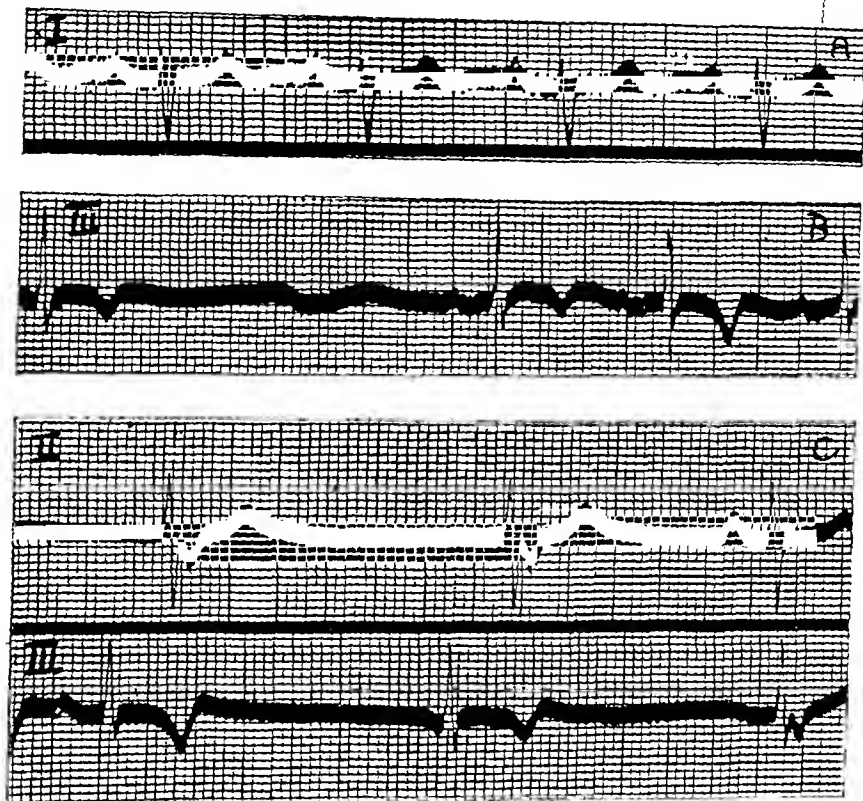


FIG. 4.—Electrocardiograms in Case 11.

- (A) Prior to administration of potassium, showing normal sinus rhythm.
- (B) 43 minutes after administration of 5g. of potassium chloride and 5g. of potassium citrate, showing period of cardiac asystole.
- (C) 71 minutes after administration of potassium, showing bradycardia with varying sites of impulse formation.

On account of the persistent bradycardia and irregularity, atropine sulphate gr. 1/50 was given subcutaneously eight minutes later, that is fifty-one minutes after the ingestion of the potassium salts, and an electrocardiogram two minutes later showed similar changes to the previous one. Others were taken subsequently, one of which, seventy-one minutes after the ingestion of the potassium salts, is reproduced in Fig. 4 C and shows a shifting pacemaker, situated sometimes in the A-V node, sometimes in the S-A node. In lead I of this electrocardiogram, which is not reproduced, ventricular complexes occur without any associated P waves. When observations were discontinued, 107 minutes after

the ingestion of the potassium salts, the ventricular rate was 72 per minute and regular. An electrocardiogram taken nearly four hours after the beginning of the experiment revealed normal sinus rhythm with the T waves still heightened; six days later another was essentially similar to the control record, and analysis of the blood showed that it was practically the same as before the administration of potassium, i.e. serum potassium 17.0 mg., serum calcium 10.5 mg. and blood urea 42 mg., in each case per 100 c.c.

In this patient potassium salts produced changes in intracardiac conduction, just over forty minutes after their ingestion, changes which the electrocardiogram showed, consisted principally of suppression of the sinus as the inaugurator of the cardiac impulse, this function being finally taken over by either the A-V node or bundle. Two points of interest are that conduction in the ventricles was not affected, and that when the sinus again took over its normal function as pacemaker there was no evidence of more than a very slight delay in conduction between the auricles and ventricles.

(C) OTHER SIGNS OF TOXICITY

Apart from the effects on the heart just described, few definite signs of toxicity were observed from giving potassium salts. All the patients disliked the taste of the chloride mixture, a taste which it is wellnigh impossible to disguise. Vomiting occurred in five patients, but generally in those with malignant hypertension or chronic nephritis, in whom the least disturbance was liable to produce vomiting, and in only one of these was it persistent. Only one patient complained of symptoms that might be cardiac, namely thumping of the heart. Three, including the two described in the preceding section, complained of tingling in the arms and legs followed by a sensation as if the limbs were dead or heavy; and sweating occurred in one. Diarrhœa was not encountered in any of the patients.

DISCUSSION: (A) POTASSIUM AND THE T WAVE

During the last sixty years the effect of the inorganic cations, including potassium, upon the heart has been very fully studied by the physiologists, notably Ringer (1880-82), Howell (1899, 1902, 1905-06), Greene (1899), Hald (1905), and Hering (1915). All these, however, have made use of the experimental animal, including the frog, rabbit, cat, and dog, and little work has been done upon the effects of these cations on the human heart, the inference having been accepted that comparable effects might be expected in the case of man.

One of the few investigations carried out in man is that of Harris and Levin (1937), who injected various amounts of a 5 per cent. solution of potassium chloride into six normal subjects and reported that the height of T was sometimes increased, but that "no definite correlation could be found between the magnitude of the changes in the electrocardiogram and the concentration of potassium in the blood stream." The two most direct studies with the experimental animal have been those of McLean and his colleagues (1933) and of Winkler and his colleagues (1938). The former, working with the perfused rabbit's heart, showed that increasing the potassium content of the perfusing fluid resulted in a high T wave, and diminution in a low or negative T wave.

Winkler, Hoff, and Smith (1938) injected isotonic solutions of potassium chloride intravenously into dogs and found that the first change to occur was an increase in the height of the T wave, which progressed until T equalled the QRS complex in amplitude. Wiggers (1930) also has shown that the intravenous injection of potassium chloride in the dog is followed by a pronounced increase in the height of T.

It is not proposed here to discuss all the factors that are known to cause an increase in the height of the T wave, but some of them appear to have a bearing on the present problem, and among these one of the most important is the effect of asphyxia on the heart. As has been shown by D'Silva (1934) and Cattel and Civin (1938) in the case of the cat, and by Dennis and Mullin (1938) in the case of the dog, asphyxia results in an increase in the concentration of the serum or plasma potassium. Most workers are agreed that asphyxia results in an increase in the height of the T wave. Thus Greene and Gilbert (1922), producing anoxæmia in dogs by a rebreathing method, found that as the anoxæmia developed the most typical change in the electrocardiogram was that T became increasingly taller till it was as high as the original R wave, and that this change "apparently did not depend on a change in the position of the heart." Similar results were obtained in dogs by Haggard (1921), and Kountz and Hammouda (1932), working with a heart-lung preparation in the same animal, found that excess of carbon dioxide increased the height of T in all leads.

Similar changes in the T wave have been obtained in alkalosis and acidosis. Barker, Shrader, and Ronzoni (1939) found in man that alkalosis resulted in a lowering of the T wave, the opposite effect being produced by acidosis. In dogs Schott (1926) reported that the intravenous injection of hydrochloric acid was followed by a rise, and of sodium bicarbonate by a fall in the height of the T wave. Carter, Andrus, and Dieuaide (1924) found that upright T waves in the cardiogram of a dog being perfused with a solution of pH 7.1 became negative when the reaction of the perfusate was made less acid (pH 7.4.) Allott and McArdle (1938) report that in a severe case of tetany and alkalosis due to vomiting from pyloric obstruction the serum potassium was as low as 7.6 mg. per 100 c.c., which is of interest in this connection.

Pitressin has also been shown to cause an increase in the height of the T wave in dogs (Resnik and Geiling (1924-25), Gruber and Kountz (1930), and Melville (1938)), and this and the other effects on the heart have been attributed by these authors to anoxæmia of the heart. D'Silva (1934) found that pitressin caused a rise in the serum potassium.

In view of these findings, namely that an increase in the height of the T wave is caused by asphyxia, acidosis, pitressin, and potassium, taken in conjunction with the correlated changes in the level of the serum potassium, there would seem to be some justification for the hypothesis that the common factor—potassium—may be the cause of these changes. Andrus and Carter (1924) in their work on the effect of changes in pH upon the heart suggested that these changes might be elicited by a disturbance of ionic equilibrium between the cell contents and the tissue fluid, and, in view of the fact that potassium is dominantly an intracellular ion, it is only to be expected that any such dis-

turbance of ionic equilibrium might be accompanied by an increase of potassium in the extracellular fluids, including the bloodstream. Whether potassium acts directly or indirectly, and the mechanism of its action are questions which can be discussed more conveniently in association with the changes produced in intracardiac conduction.

(B) POTASSIUM AND CONDUCTION

As the two cases just described show, the effects of potassium on the heart in man are comparable with those in the experimental animal, the main difference being that in man there is much less effect on the ventricle. This is probably due to the fact that much larger amounts are needed to affect the ventricle in man than it would be possible to give with safety.

The problem which is of outstanding interest here is the mechanism whereby potassium produces these effects. Is the block due to a direct effect of potassium upon the myocardium, or is it an indirect effect mediated through the vagus? That there is a close association between the effects of the vagus and of potassium on the heart has been suggested by many workers since the original work of Howell (1905-06) who showed in frogs and terrapins that an increase of potassium in the circulating medium enhanced the sensitiveness of the heart to vagus inhibition, and interpreted these results as meaning that the vagus impulses act indirectly by increasing the amount of diffusible potassium compounds in the heart tissue. Subsequently (Howell and Duke, 1908) he found that in the isolated mammalian heart stimulation of the vagus caused an increase in the potassium content of the circulating medium. Among more recent workers who have confirmed these findings may be quoted Herz (1935) who found that potassium ions have a marked effect upon the sensitivity of the heart of the frog to vagal stimulation, and Lenhartz (1936) who found in the isolated auricle of the tortoise an increase in the potassium content of the perfusion fluid following stimulation of the vagus.

A similar close association has been shown to exist between acetylcholine and potassium. Thus in the heart of the frog, Chang and Gaddum (1933) found that potassium produced effects similar to those given by acetylcholine. In the cat, Brown and Feldberg (1936) found that potassium increased the response of the superior cervical ganglion to preganglionic stimuli and liberated acetylcholine from the ganglion, while Feldberg and Guimarães (1936), finding that intra-arterial injections of potassium chloride liberated acetylcholine from various organs, consider this supports the suggestion that discharge of acetylcholine may be effected by potassium ions mobilized in the passage of the nerve impulse. Fischer (1936) has suggested that different vagal fibres affecting the heart are not only functionally different, but that there exist several chemical transmitters for the vagal action, one of which is potassium and another acetylcholine.

Further light is thrown on the problem by the careful study of Greene and Gilbert (1922) of the effects of anoxæmia on the heart. Working with the dog and producing a gradually increasing anoxæmia, they found that this inhibited sino-auricular rhythm or drove the rhythm to a lower focus in the

tail of the sino-auricular node. When sino-auricular rhythm was inhibited, an auriculo-ventricular rhythm became dominant, but at a slower rate. If at this stage the anoxæmia was relieved, normal rhythm was restored, but, if the anoxæmia was allowed to develop, the rhythmic centre was driven down into the left bundle branch. Section of both vagi invariably abolished these early changes and was followed by the onset of sinus tachycardia. They therefore concluded that the early anoxæmic changes were a vagal effect, and that it was only when an extreme degree of anoxæmia was produced that suppression of rhythm was obtained due to cardiac anoxæmia. Their criticism of other workers, such as Mathison (1910-11), who considered that the heart block of asphyxia was not due to a vagal effect, was that these workers had used such rapid methods of inducing anoxæmia that they missed the early stage of slowing due to the vagus and only obtained the late stage of direct cardiac anoxæmia. The interest of these findings of Greene and Gilbert is that the changes they produced in the heart were very similar to those obtained in our second case. In both instances there was suppression of the sino-auricular node as pacemaker, the auriculo-ventricular node taking on this function, and in both the first change was a heightening of the T wave. It was on these grounds that atropine was administered at the height of the block in our case, but in view of our ignorance as to how long the potassium effect persists it is not possible to decide whether the return of normal sinus rhythm was due to the atropine or not.

In other words we find that vagal stimulation and acetylcholine and potassium all produce the same effects on the heart, and that the two former increase the extracellular concentration of potassium. Further Lenhartz (1936) has shown in the isolated auricles of the heart of the tortoise that when enough atropine is present to suppress the inhibitory action of vagal stimulation and of acetylcholine, neither of these last procedures produced any change in the concentration of potassium ions. There would therefore seem to be justification for advancing the hypothesis that these particular changes in the function of the heart are mediated through the action of the potassium ion. The exact mechanism of this action still awaits further elucidation.

CLINICAL APPLICATIONS

While the pathological aspects of the relationship of potassium to cardiac pathology raise many interesting problems, with which it is not intended to deal here, there is a clinical aspect, now being investigated, which would seem to be worthy of attention.

Potassium salts, particularly in the form of the citrate, have long enjoyed a reputation as diuretics both in renal and cardiac œdema. The dose of potassium citrate, according to the British Pharmacopœia, is 10-60 grains (0.65-4 g.). Potassium chloride is included in the British Pharmaceutical Codex, where the dose of this salt is given as 15-60 grains (1-4 g.). As a rule, however, much larger doses are prescribed. Thus Blum (1920) gave 25 g. of the chloride daily in cases of chronic nephritis, while Osman (1927) gave his patients with Bright's disease 24 g. of potassium salts (12 g. of citrate and 12 g. of bicarbonate) daily. Keith and Binger (1935) recommended a standard daily dose equivalent to

5 g. of potassium (10 g. of chloride or 14 g. of citrate), and even larger amounts were given by Hawes and Vardy (1935) in nephrosis, a mixture containing 2 g. of potassium bicarbonate and 2 g. of citrate, every hour for long periods.

The general assumption has been that large doses of potassium salts by mouth are not toxic on account of the rapidity with which they are excreted in the urine. To quote the British Pharmaceutical Codex (1934), "Potassium chloride does not exhibit the depressant action of the potassium ion on the tissues, because it is excreted with such extreme rapidity that the blood never contains it in sufficient concentration to produce the specific effect." That this is not always the case, however, is shown by the figures in our cases, and particularly is this so in chronic nephritis, the very group in which potassium salts are usually administered as diuretics. In view of the marked disturbances which can be produced by the ingestion of potassium salts by mouth, their administration in patients with cardiovascular disease would seem to be contra-indicated, or at least they should only be given in small doses. A consideration of the treatment of the large number of elderly patients with enlargement of the prostate, who are given mixtures containing anything from 4 g. (60 grains) of potassium citrate three or four times a day both before and after operation, raises the interesting question as to the effect of such medication on a heart that is often far from healthy. Is this the solution of the problem as to why some of these patients occasionally die suddenly?

A further clinical application is suggested by Camp's (1939) work on the potentiation of digitalis action by potassium. This investigator found in dogs that the administration of three or four doses of digitalis given every five minutes was without effect on the pulse or amplitude. If potassium chloride was given at this stage, however, marked slowing of the pulse occurred accompanied by an increase of amplitude. He suggests that digitalis exerts an early unrecognizable action on the heart which can be made manifest by potassium.

SUMMARY.

1. Potassium salts, in the form of the chloride and the citrate in doses varying from 3-30 g. daily, have been given to twenty-four patients with various diseases, and the effect on the electrocardiogram has been observed.

2. In fourteen of these the administration of potassium salts was followed by an increase in the height of the T wave in one or more leads. No correlation was found between the increase in the height of the T wave on the one hand and the amount of potassium given or the increase in the concentration of the serum potassium on the other, except that in the fourteen patients who showed this change the average increase in the level of the serum potassium was 8.3 mg. per 100 c.c., compared with 2.6 mg. per 100 c.c. in the patients who showed no such change.

3. In one patient the T wave, which was diphasic in all leads before the administration of potassium salts, became more deeply diphasic while they were being given.

4. In two patients definite degrees of heart block were produced by the administration of potassium salts. In one, there was prolongation of the P-R

interval, while in the other sino-auricular block and nodal rhythm resulted with marked slowing and irregularity of the heart rate.

5. The similarity of these changes to those produced by vagal stimulation, by acetylcholine, and by pitressin is discussed, and the hypothesis is advanced that in each case they may be mediated through the action of the potassium ion on the myocardium.

6. Certain clinical applications of this work are also discussed, and it is recommended that potassium salts should be used with the utmost caution in patients with cardiovascular or renal disease.

I am indebted to Professor O. L. V. S. de Wesselow for permission to carry out these investigations on patients under his care and for the interest which he has taken throughout this work.

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THE ÆTIOLOGY OF LUNG INFARCTION

BY

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The purpose of this communication is to try to show that the common hæmorrhagic infarct of the lung is usually an embolic rather than an autochthonous phenomenon. This is by no means a new idea; as will be evident enough from Ceelen's (1931) exhaustive review of the subject. But the alternative view, which supposes the pulmonary arteries to be a common site of autochthonous thrombosis, is still widely prevalent.

This report is concerned with a series of 1990 consecutive autopsies in which special attention has been given to dissection of the pulmonary arteries. These autopsies, as a series, may be regarded as fairly representative of general hospital cases. More than half of them were performed in the Department of Pathology at the University of Toronto from 1931 to 1936, and the rest at this School from 1937 to 1939.

There were in this series 155 cases presenting gross hæmorrhagic infarction of the lung. This was exclusive of septic infarction, for here we were concerned only with the bland, non-infective type of lesion. According to our interpretation of the autopsy findings no less than 136 of these were due to embolism, 10 only were due to thrombosis, and in 9 no definite arterial occlusion was found.

IDENTIFICATION OF EMBOLI

It is not always easy to distinguish between thrombus and embolus, but there are criteria that make it possible in most instances. The identification of an embolus may rest upon some of the following features: it may be loose-lying, coiled, jumbled, twisted, impacted (Fig. 1), or riding a bifurcation; it may have a branching conformity that does not correspond with that of the vessel in which it lies, or it may have freshly broken ends. More important perhaps than its shape and location is the quality of the clot. The type of embolus with which we are concerned is usually a red clot composed chiefly of fibrin and red blood cells. Because it takes origin in slowly moving or stagnant venous streams, it is not unlike the clot that freshly drawn blood will form on standing in a test tube. On the other hand, thrombus that takes origin in the pul-

monary arteries is usually white or light pink, and composed chiefly of platelets and white cells, because it is laid down in a faster moving stream. It is always attached more or less securely to the vessel wall. It usually has a sessile base with gently shelving margins, and it is moulded to the shape of the vessel in



FIG. 1.—Embolus in a tertiary branch of the pulmonary artery. It looked like an autochthonous thrombus until it was hemisected, as seen here, when its jumbled and distorted laminations became apparent and also the fact that it was lodged at the mouth of a smaller branch. (Museum specimen, 24.25.1, B.P.M.S.)

which it lies. If one can find in the peripheral veins a potential source for the embolism, the problem is often facilitated ; for the embolus will then resemble the parent clot.

Difficulty may be encountered when both embolus and thrombus are present together, but this only happens in a minority of cases. More than half of the emboli in this series occurred alone, about one-third were accompanied by small amounts of autochthonous thrombus, and only a few, perhaps less than five per cent., were sufficiently obscured by superadded thrombus to render their identification difficult. In such doubtful cases we have usually put it down as thrombosis.

In order to make the distinction between thrombus and embolus it is obvious that one must have a satisfactory exposure of the whole clot. To accomplish this requires a technique of dissection that will permit of opening the second, third, and even fourth divisions of the pulmonary arteries without

too much mutilation of the lungs. We have found it relatively easy to adopt such a technique (Belt, 1936) as a routine procedure.

HÆMORRHAGIC INFARCTION OF THE LUNG

The following table indicates the nature of the 155 cases in which infarcts were found.

TABLE I
ANALYSIS OF HÆMORRHAGIC INFARCTION OF LUNG

Certifiable Cause of Death	Cause of Infarction			
	Embolism	Thrombosis	Unknown	Total
Heart disease	70	3	1	74
Pulmonary embolism	22	—	—	22
Malignant neoplasm	17	2	2	21
Pulmonary tuberculosis	8	1	—	9
Cerebral softening	8	1	2	11
Various	11	3	4	18
Total number of cases	136	10	9	155

CASES WITH EMBOLIC INFARCTS

Pulmonary embolism was regarded as the main cause of death for purposes of certification in 22 cases, and as a contributory cause in 77; the remaining 37 of the 136 cases were examples of minor embolism, some of them showing only a single infarct.

Of all the pulmonary emboli encountered in this series of 1990 autopsies, not more than half were associated with infarction; that is to say, there were about twice as many cases of embolism as of infarction. Since Virchow's time it has been well known that occlusion of a pulmonary artery is in itself insufficient to produce an infarct. There must be added factors, and it cannot be said that we know precisely what these are; nor does it lie within the scope of this paper to define them. Certain it is, however, that heart disease outshadows all other conditions as a concomitant of lung infarction. The theoretical explanation is that any lesion retarding the normal flow of blood through the left auricle produces increased pressure in the pulmonary veins, and this may lead to complete stasis and necrosis (hæmorrhagic infarct) in the event of an arterial occlusion.

In this series of 1990 autopsies there were 235 deaths registerable as from heart disease. The majority of them had congestive failure. Almost a third (70 cases) died with embolic infarcts of the lungs. Table II gives a survey of these.

There were 27 cases of rheumatic disease, 24 with mitral stenosis; with an average age of 39 years. An equal number had coronary disease, 21 with

coronary occlusion (old or recent) and 16 with angina pectoris; their average age was 63 years. The remaining 16 were miscellaneous cardiopathies, with an average age of 54 years.

The second largest group in Table I consists of 22 cases of sudden death from pulmonary embolism. Twelve were recovering from operations (9 laparotomies and 3 prostatectomies), 7 from fractures (5 of the femur, 1 of the pelvis, and 1 of the ribs), and 3 were medical cases in which the embolism arose more or less *de novo*.

TABLE II
SEVENTY CASES OF HEART DISEASE WITH EMBOLIC INFARCTS

Certifiable Cause of Death	Number of Cases				
	Total	With Congestive Failure	With Major Embolism *	Clinical State	
				Bed-ridden	Ambulatory
Rheumatic heart disease ..	27	25	21	20	7
Coronary disease ..	27	18	18	19	8
Other cardiopathies	16	9	8	12	4
Total	70	52	47	51	19

* Pulmonary embolism severe enough to be entered on the death certificate as a contributory cause of death.

The interval between operation and death varied from three to seventeen days and averaged eleven days. In the fracture cases the interval averaged twenty-two days. Infarction of the lung is not uncommon in deaths from pulmonary embolism after operation or after trauma, and indicates, as a rule, that smaller emboli have preceded the fatal seizure by hours or days.

It was possible to find the *apparent source of the emboli* in 116 cases. Usually it was a thrombus in the veins of the pelvis or thigh. The actual figures, as shown in Table III, were: pelvic veins 52, leg veins 42, right heart 16, veins of upper extremity (including subclavian) 6.

In the pelvis the commonest sites were the peri-prostatic, the uterine, and the internal iliac vein; in the thigh, the femoral and saphenous veins.

Seldom was the venous thrombosis accompanied by obvious phlebitis and this, of course, is a factor which tended to obscure the clinical recognition of embolism in many of our cases. Perhaps the commonest and most distinctive symptom recorded in the histories of these cases was the coughing up of blood, either as rusty sputum or as frank hæmoptysis. In addition, pleural pain and pleural rubs were frequently observed. Under such circumstances the infarction was commonly mistaken for pneumonia with pleurisy. Another common

symptom was a sudden attack of breathlessness, accompanied by cyanosis, anxiety, and sweating; and this was often put down to a sudden change for the worse in the function of the heart rather than to embolism.

TABLE III
APPARENT SOURCE OF EMBOLI

Certifiable Cause of Death	Thrombus in				
	Pelvic Veins	Leg Veins	Arm Veins	Right Heart	All Sites
Rheumatic heart disease	7	6	5	5	23
Coronary disease	11	8	—	5	24
Other cardiopathies	6	5	1	4	16
Pulmonary embolism	8	10	—	—	18
Malignant neoplasm	10	5	—	—	15
Pulmonary tuberculosis	1	3	—	2	6
Cerebral softening	4	3	—	—	7
Miscellaneous	5	2	—	—	7
All Causes	52	42	6	16	116

PRIMARY PULMONARY THROMBOSIS

The ten cases of pulmonary thrombosis were of miscellaneous origin and scarcely permit of generalizations. In two instances there was tumour invasion of the vessel wall and in a third an arteritis due to tuberculous disease of the lung. Three others had small thromboses as a concomitant of severe toxæmia. In the remaining four the thrombosis was probably attributable to antecedent embolism.

Endarteritis of the pulmonary arteries has often been cited as a cause of pulmonary thrombosis, but in my experience this is rare. What may sometimes be mistaken for endarteritis is an involutional change in a vessel wall beyond a point of embolic occlusion. It is something like the change that occurs in the umbilical artery after birth. The intima proliferates to a considerable thickness (Fig. 2) and might well be taken for endarteritic change, if one did not know the vessel had been rendered defunct by an embolus lying proximal to the point where the section was taken.

DISCUSSION

Virchow (1856) introduced the term embolus and first described the phenomenon of thrombo-embolism; he said that ante-mortem clots in the



FIG. 2.—Intimal thickening in a pulmonary artery, distal to the point of embolic occlusion. This change, which is involutional, may be mistaken for endarteritis. Magnification, $\times 30$. (Museum specimen, 152.25.2, B.P.M.S.)

pulmonary arteries were, in his experience, practically always embolic, and that their occurrence was an almost sure indication of older thrombus somewhere in the venous circulation. Others who have carried out large scale investigations on autopsy material have reached a similar conclusion (Lubarsch, 1905; Möller, 1922). Ribbert (1902) seems to have been the chief protagonist of the alternative view. His grounds for dissent seem somewhat obscure, but he denied the importance that Virchow attached to embolism and held the majority of pulmonary clots to be formed *in situ*. Ribbert's teaching became firmly established in the minds of many of his followers and to this day it is not easily shaken. My former chief, the late Professor Oskar Klotz, was one of Ribbert's students, and it was only after painstaking examinations in a large series of autopsies (Belt, 1934) that he became convinced of the relative frequency of embolism.

One would find it difficult to decide between the conflicting views of Virchow and Ribbert without putting the matter to an actual test. The important point is : What are the criteria by which an embolus may be recognized ? There are perhaps no hard-and-fast criteria, and those which have been set down here may be as arbitrary as any yet devised. On paper one can but convey a general impression of how an embolus is identified ; in practice it becomes relatively easy provided a satisfactory dissection of the pulmonary arteries is carried out.

If, as we suppose, 85 per cent. or more of lung infarcts are due to embolism,

then the problem of ætiology is largely a consideration of venous thrombosis, and that is a matter which remains obscure. In another place (Belt, 1939) I have indicated that most cases of thrombo-embolism present evidence of a prolonged circulation time, and I have emphasized again the mechanical factors to which Aschoff drew attention years ago—stasis, stagnation, and eddying—as important in the causation of the embolizing type of thrombus.

SUMMARY

In 1990 consecutive autopsies on adults, there were 155 cases of hæmorrhagic infarction of the lung. Pulmonary embolism was regarded as the immediate cause of 136 (approximately 87 per cent.) of these infarcts.

In 22 (14 per cent.) a massive pulmonary embolism was the main diagnosis, and most of these were after operations or fractures. In 74 (47 per cent.) heart disease appeared to be a predisposing factor.

A potential source of emboli was demonstrated in 116 (75 per cent.) of the infarct cases.

Means of identifying emboli at autopsy are discussed, and evidence adduced to show that embolism of the pulmonary arteries is of very common occurrence, while primary pulmonary thrombosis is relatively rare.

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NOTE BY THE EDITOR

A recent paper by H. J. Atkins (*Guy's Hospital Reports*, 88, 92, 1938), dealing with post-operative thrombosis and embolism, reaches the same conclusion that pulmonary infarction is nearly always caused by embolism from venous thrombosis. He finds that massive embolism may occur any time in the first fifteen days, most often about the tenth day; and that it is independent of sepsis, and therefore depends on the stagnation of the blood stream, especially from the mechanical conditions of rest. Smaller infarcts

are more closely associated with sepsis (which suggests that the embolism is more often due to the breaking off of a small part of the thrombus), and are more erratic in the time of their appearance. He emphasizes the importance of the pressure of the right common iliac artery on the left common iliac vein in producing the thrombosis. His figures cannot be given in detail here, but are interesting in comparison with the relevant figures of Belt.

HERPES ZOSTER AND ANGINA PECTORIS

BY

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Substernal pain on effort is recognized as one of the manifestations of disease of the coronary arteries. However, in recent years, clinicians have come to recognize the coronary nature of attacks in which pain is absent or minimal. That pain of cardiac origin is not necessarily paroxysmal has also been suggested, while occasionally painless symptoms have been recognized to accompany or even to replace true anginal pain. In a future paper the authors propose to describe such phenomena and consider their significance. In this communication we shall consider one such phenomenon, namely, herpes zoster, and its occurrence in patients with angina pectoris.

Several observers have noted the occurrence of herpes zoster in patients suffering from periodic bouts of anginal pain. A study of the case histories in Head's (1900) classical report on herpes zoster revealed that one of his patients was suffering from anginal paroxysms. He was a man of 35 years, with weakness and cough of two years' duration and severe attacks of pain over the heart. Herpes zoster developed over his chest on the right side, at the level Th. 7, one week before his entry to hospital. He died on the following day during a severe anginal attack and at autopsy proved to have extreme atheroma of the aorta, with aortic obstruction and regurgitation, and an enlarged left ventricle. No mention was made of the coronary arteries. The right Th. 7 ganglion was profoundly affected, riddled with extravasated blood and round-cell infiltration. Head did not consider the possible significance of the association of the two conditions. Osler, in his Lumleian lectures on angina pectoris (1910), mentioned a patient who developed herpes zoster along the track of the anginal pain he had felt periodically for the previous ten years; it was the only such case that Osler had witnessed. Allbutt (1915) observed two cases in which the conditions were associated and wrote, "In the case of a lady (suffering from angina pectoris) who arrived at my house after an attack (of herpes zoster), the left arm had to be gently borne on a pillow by her maid as she passed from the carriage to the house."

With one exception, remaining references on this subject are of German origin. In Ortnier's patient (1911) the zoster was distributed over the area subserved by the left ulnar nerve, Th. 1; such a distribution is uncommon

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(Head, 1900). The patient had been suffering from genuine angina pectoris for some time and the pain radiated down the ulnar aspect of the left arm in attacks. Autopsy showed intense sclerosis of the coronary arteries without evidence of syphilis of the aorta or elsewhere. Fehsenfeld (1921) has described a similar case. Arnstein (1921, 1922) observed the association of herpes and angina, and in a paper entitled "Herpes zoster as the only manifestation of affections of internal organs running an otherwise latent course" concluded that zoster is frequent with disease of the lungs, liver, and kidneys, while rare with digestive, genital, and heart disease. He observed that its location usually corresponded with the organ affected. In one patient with marked sclerosis of the abdominal aorta attended with paroxysms of severe colicky abdominal pain, herpes zoster appeared over the left upper quadrant. Wertheimer (1927 and 1928) reported two patients with paroxysms of angina pectoris, of one and eight years' duration respectively, who developed herpes zoster over the area of radiation of substernal and arm pain. In one it occupied segments Th. 1-4 anteriorly and posteriorly on the left side, and segment Th. 1 on the left arm. In the second the arm was not involved by the rash, but the thumb and index finger of the left hand began to show diminished sensibility to pain. Parsonnet and Hyman (1930) have recorded three interesting cases in which recurrent attacks of herpes zoster were associated with the simultaneous development of symptoms and signs of progressive coronary disease, as evidenced by typical anginal seizures, electrocardiographic changes, and ultimate sudden death in all three. Previous to the first bouts of herpes zoster there were no cardiac symptoms or signs and electrocardiograms taken at the time of the herpes attacks proved normal.

We have encountered 12 instances of herpes zoster in a series of 350 patients with angina pectoris. In 10 instances the zoster appeared after the anginal attacks had become established, while in 2 the zoster preceded the angina. In the latter (Cases 11 and 12) the zoster first appeared before the first anginal paroxysm. In Case 11 the subsequent anginal pain involved the right shoulder and arm, where the zoster rash had appeared two and a half years before. In Case 12 there were recurrent attacks of herpes zoster over the left chest in the eighteen months preceding the first anginal attack. In the remaining 10 cases the anginal pains had been experienced first, in all but one for several years, and in the majority were severe and frequent.

The main features of these 12 cases are outlined in Table I. The majority of patients were elderly, 8 being over sixty years of age. All suffered from true angina of effort, relieved by nitrites, except one (Case 10), who had a syphilitic aneurysm of the ascending limb of the arch of the aorta with much substernal and left arm pain. The Wassermann and/or the Hinton reactions were negative in the remainder, and none gave a history of luetic infection. Electrocardiograms, taken in six cases, all showed evidence of coronary insufficiency.

In Figs. 1 to 12 are outlined the distributions of the referred cardiac pain and herpetic eruption in the 12 patients, and short histories follow. In 10 cases a fairly close segmental relationship is apparent between the two areas. In

Case 6 the cardiac pain was referred to the right shoulder and arm (C. 5, 6, 7, 8 and Th. 1, 2, 3) while the eruption appeared over the left shoulder (C. 4). In Case 9 the anginal pain was very severe and widespread; it radiated to both shoulders and arms and occasional paroxysms spread to involve the epigastrium, left upper quadrant of the abdomen and the left infrascapular region. The eruption commenced on the anterior aspect of the left thigh and spread upwards over the left inguinal and gluteal region to involve the left lumbar area (Th. 9, 10, 11, 12 and L. 1 and 2).

TABLE I
HERPES ZOSTER AND ANGINA PECTORIS

Case Number	Age in Years	Number of Years with Angina before the Onset of Herpes	Site of Anginal Pain	Severity of Angina	Frequency of Angina	Distribution of Herpes
1	74	4	Substernal to R. and L. upper chest	XXX	Daily	Right : Th. 5, 6, 7. Anterior.
2	70	4	Præcordial to L. shoulder	XXX	Irregular Infrequent	Left: Th. 2, 3, 4. Anterior
3	67	6	Substernal to L. chest and shoulder	XX	Frequent	Left : Th. 2, 3, 4. Ant. and Post.
4	60	2	Substernal to R. chest	XX	Frequent	Right : Th. 6, 7. Ant. and Post.
5	54	5	Substernal	XX	Frequent	Left : Th. 5, 6. Ant. and Post.
6	83	12	Substernal to R. arm	XX	Frequent	Left : C. 4. Anterior.
7	70	1½	Substernal to R. arm	XXX	Frequent	Right : C. 4, 5. Th. 1, 2, 3, 4. Anterior.
8	58	4	Substernal	XXX	Very frequent	Left : C. 5, 7, 8. Th. 1, 2. Anterior.
9	66	5	Substernal to both arms	XXX	Very frequent	Left: Th. 9, 10, 11, 12. L. 1, 2. Anterior.
10	42	5	Substernal to left axilla and neck	XX	Very frequent	Left : C. 4, 5, 6. Anterior.
11	49	*	Substernal to R. arm	XX	Frequent	Right : Th. 4, 5, 6. Anterior.
12	71	*	Substernal to L. arm	XX	Frequent	Left : Th. 4, 5, 6. Anterior.

XX signifies moderate anginal pain.

XXX signifies severe anginal pain.

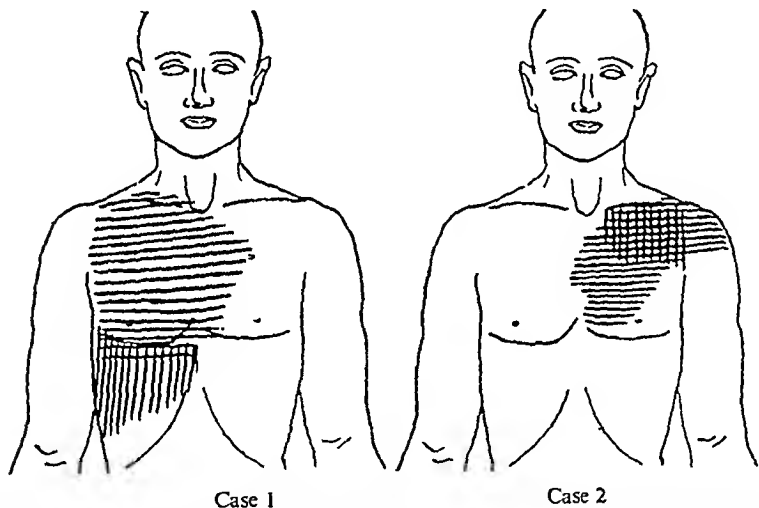
* In these two cases the herpes occurred 2½ and 1½ years respectively before the angina.

CASE HISTORIES

Case 1.

Male, aged 74. Left temporal headaches for five years. Four years dyspnoea on exertion and typical angina of effort, lasting a few minutes and relieved by rest or nitroglycerine. There was no actual radiation of the anginal pain to the left arm, but some numbness; it spread to the upper chest on both sides, chiefly the right. About 8 months ago, when the angina was getting more frequent and severe, an herpetic eruption appeared over the right side of the chest anteriorly, Th. 5, 6 and 7. Its lowest limit was at the costal margin approximately. He became more short of breath about this time. Three months later increasing dyspnoea and oedema of the ankles. For the past two months the anginal attacks have increased in frequency and severity.

Examination: Heart enlarged to the left by X-ray. Systolic thrill and systolic and probable diastolic apical murmurs. Radial and brachial arteries firm and tortuous. Blood pressure 160/85. Moderate oedema of ankles. Tortuous aorta by X-ray. Electrocardiogram; rate 75, fibrillating, inverted T waves in all leads, left bundle branch block.



Case 1

Case 2

FIGS. 1 and 2.—Diagram showing the areas of distribution of the herpetic eruption and of the referred cardiac pain. The black horizontal lines indicate the area of the referred pain and the vertical lines represent the distribution of the herpetic eruption.

Case 2.

Male, aged 70. Well and active until four years ago, when first attack of præcordial pain on walking. Tends to recur on excitement or exertion. One year ago a severe attack without radiation to arms. Hypertension then present. Two months ago herpes zoster over the left chest and shoulder. Unable to continue his work as a butler thereafter.

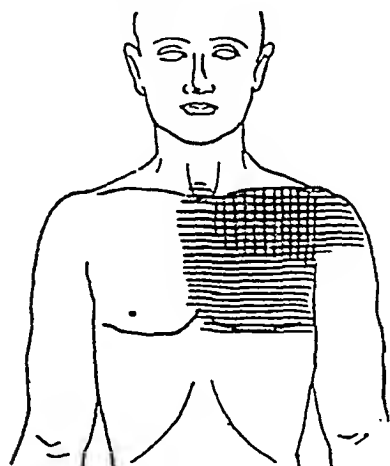
Examination: B. P. 180/90. Slight apical systolic murmur; soft arteries; liver edge felt one finger below costal margin; slight oedema of ankles.

Case 3.

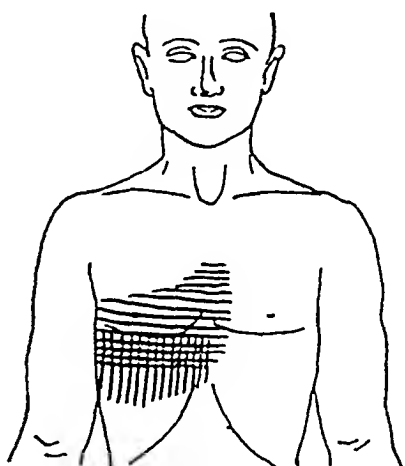
Male, aged 67. Six years headaches, palpitation, and weakness, and started to have dyspnoea and substernal distress on exertion: unable to walk any distance because of this. Three days ago severe persistent pain over left chest and shoulder, without

radiation to arm. Substernal distress on exertion was particularly marked and lasted ten minutes at a time.

Examination : Obese, moderate peripheral arteriosclerosis, heart enlarged to the left with a forcible apex beat. B. P. 215/145. Systolic apical murmur. Herpetic lesions in left axilla and over upper three left ribs anteriorly, and posteriorly over left scapula. Urine, albumen and granular casts.



Case 3



Case 4

FIGS. 3 and 4.—The black horizontal lines indicate the area of the referred pain and the vertical lines represent the distribution of the herpetic eruption.

Case 4.

Female, aged 60. Two years dyspnoea and occasional substernal pain on exertion. Two days ago sudden pain starting in the right costal margin and lower chest, radiating to the right costovertebral region. This pain persisted until admission to hospital.

Examination : Slight cyanosis. B. P. 160/70. Heart enlarged to left. Systolic and diastolic aortic murmurs. Wassermann negative. Electrocardiogram ; left axis deviation, sagging T_1 and T_2 , slight late inversion of T_4 , wide slurred QRS waves, deep Q_4 , high S- T_4 . Herpes zoster over the area of pain. The patient improved, but returned one year later with persistent angina. A third admission to hospital ten years later with moderate cardiac failure and severe anginal episodes.

Case 5.

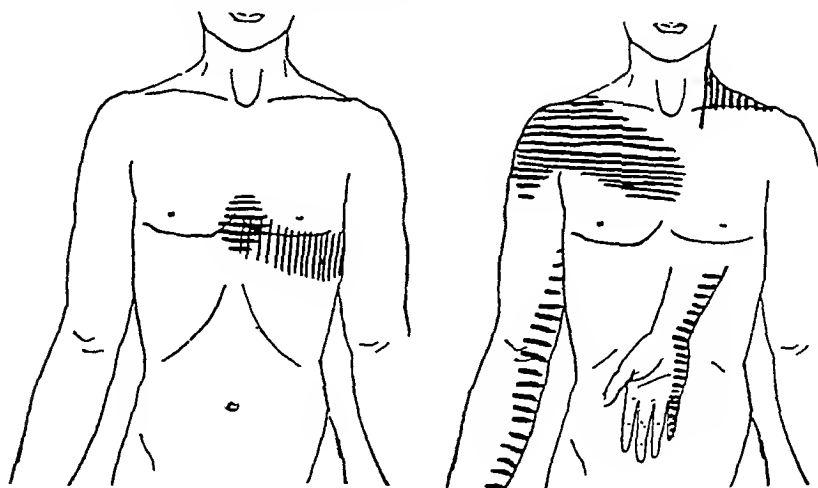
Female, aged 54. Five years ago frontal headaches and hypertension discovered. About the same time began to have substernal constriction on exertion. No radiation of pain to the arms. Attacks have persisted without much change. Five days ago superficial pain under the heart and round to the back, persistent and not in paroxysms as the anginal pain.

Examination : B. P. 260/120. Moderate arteriosclerosis. Heart enlarged to left. Blowing systolic præcordial murmur. Typical herpes over left præcordial region and at angle of left scapula. Hyperæsthetic.

Case 6.

Female, aged 83. Twelve years ago at the age of 71 severe pain in right upper chest, shoulder, and right arm on exertion. One year ago weakness and dizziness on exertion became prominent ; no præcordial pain at this time. Three days ago a typical herpes appeared over left shoulder.

Examination : Marked arteriosclerosis. B. P. 180/100. Heart enlarged to left. Apical systolic murmur. Herpetic eruption.



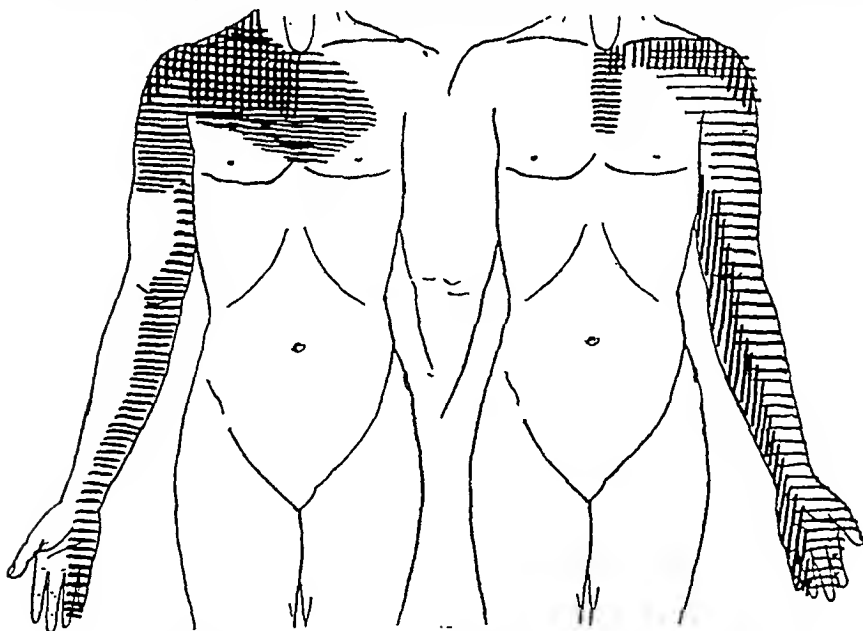
Case 5

Case 6

FIGS. 5 and 6.—The black horizontal lines indicate the area of the referred pain, and the vertical lines represent the distribution of the herpetic eruption.

Case 7.

Male, aged 70. One and a half years dyspnoea on exertion with discomfort and exhaustion ; angina pectoris diagnosed, and attacks relieved by nitroglycerine. One



Case 7

Case 8

FIGS. 7 and 8.—The black horizontal lines indicate the area of the referred pain, and the vertical lines represent the distribution of the herpetic eruption.

year ago herpes zoster over right arm, upper chest, shoulder, and neck ; still gets pain there at times, especially when resting. Six months ago typical anginal attacks with radiation of pain to the right shoulder and arm.

Examination : Poor, distant, heart sounds. Apical systolic murmur. Sclerosed radial artery. Rales at both lung bases : liver edge tender, two fingersbreadth below costal margin ; no œdema.

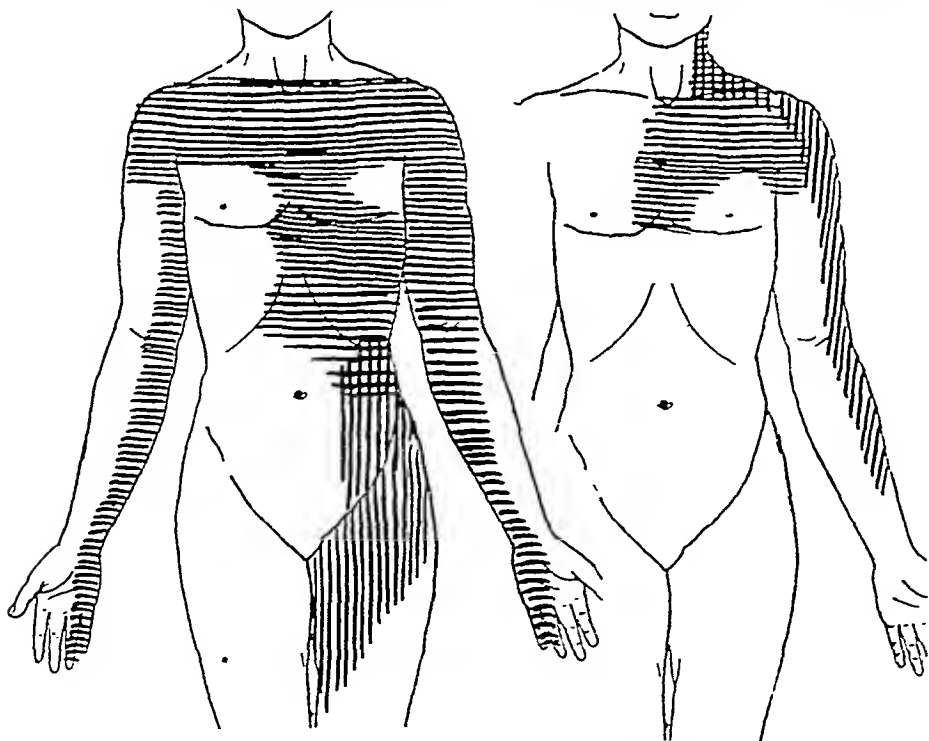
Case 8.

Male, aged 58. Four years ago midsternal pain on exertion, relieved by rest, or nitroglycerine. Increasing in frequency and severity. Three years ago in hospital : heart enlarged to left, with distant heart sounds. Rough apical systolic murmur with (?) diastolic aortic murmur. Liver just palpable. Electrocardiogram ; normal rhythm, low T_3 , inverted T_4 . Fairly well for the next three years. Last three months angina pectoris much worse, but still relieved by nitroglycerine. Two weeks ago more severe pain in left shoulder, radiating to the left arm and fingers. At first only present on exercise but soon became constant. Nitroglycerine ineffective. At this time the substernal anginal pain on exertion radiated to the left arm and left fingers, for the first time. No dyspnœa.

Examination : As before. B. P. 180/90. Typical herpes scattered over left shoulder and down the inner side of left arm to fingers. The painful area radiating from the sternum spread down the outer side of that arm. Gradual improvement.

Case 9.

Male, aged 66. Five years typical anginal attacks ; pain severe and widespread, to both arms, to epigastrium and left loin. Nitroglycerine gave prompt relief.



Case 9

Case 10

Figs. 9 and 10.—The black horizontal lines indicate the area of the referred pain and the vertical lines represent the distribution of the herpetic eruption.

Typical gout for some years. Four days ago sudden sharp shooting pain in left side of lower chest, loin, and left thigh. This was quickly followed by an herpetic eruption.

Examination : Obese. Herpes as described. Heart enlarged to left ; premature beats ; apical systolic murmur. Moderate arteriosclerosis. Electrocardiogram ; diphasic T_1 .

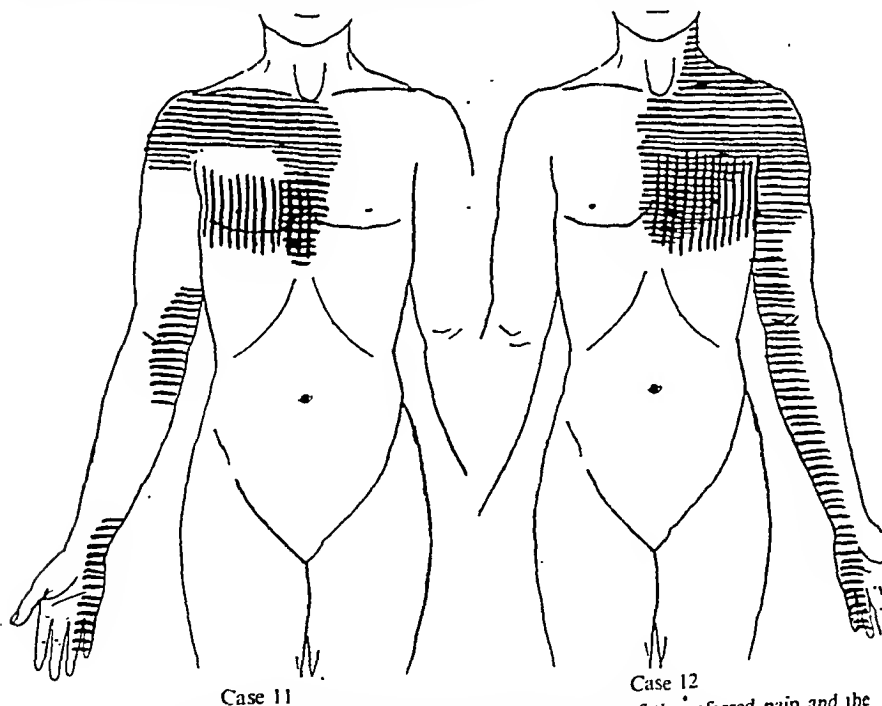
Case 10.

Male, aged 42. Five years præcordial pain with cough, dyspnœa, and dysphagia. Wassermann reaction positive. Aneurysm of aorta on X-ray. Treated with mercury and iodides. Now almost constant chest pain and anginal exacerbations. Aneurysm pointing in the suprasternal area. Two weeks ago hyperæsthesia over the left upper chest with severe, sharp, burning pain. Five days ago herpes zoster over left upper chest, axilla, and radial aspect of left arm.

Case 11.

Male, aged 49. Four years ago attack of herpes zoster involving the right chest and arm ; no sequelæ. Eighteen months ago some stabbing pain in left chest. Six months ago typical angina with pain down right arm. Attacks progressive and excruciating and one lasted for 36 hours.

Examination : Raised temperature and leucocytosis of 14,000. B. P. 115/70. Electrocardiogram ; inverted T_1 and T_4 , wide slurred QRS waves. Following this myocardial infarction, recurrent anginal attacks. Heart slightly enlarged.



FIGS. 11 and 12.—The black horizontal lines indicate the area of the referred pain and the vertical lines represent the distribution of the herpetic eruption.

Case 12.

Male, aged 71. Recurrent attacks of herpes zoster over the left mid-chest region. front and back, during several years ; scars present under the left breast. Typical

attacks of angina pectoris for eighteen months beginning substernally and spreading to left upper chest, shoulder, and ulnar aspect of left arm. Attacks provoked by exercise, emotion, or a heavy meal; four or five attacks daily of late.

Examination: Moderate peripheral arteriosclerosis. B. P. 160/100. Heart enlarged to left, fair heart sounds, no murmurs. Palpable liver edge. Tortuous aorta on X-ray examination. Electrocardiogram; diphasic T_2 and T_3 .

DISCUSSION

Are these findings fortuitous or does the zoster reflect some change in the posterior root ganglia in anginal patients? Having sifted the available evidence we lean to the latter explanation and suggest that the zoster is a trophic manifestation of continued irritation of the posterior root ganglia by impulses from the diseased viscus. Our evidence may be marshalled as follows.

As we have pointed out, the phenomenon has been recorded previously. The discovery of twelve examples among our own records is significant. A rapid control perusal of a large number of case histories of congestive heart failure revealed no example of herpes zoster in the same age group. The similarity between the relative areas of distribution of the referred cardiac pain and the herpetic rash is so striking in several instances that coincidence seems highly improbable. In Case 7 (Fig. 7) both were distributed over the right upper chest and inner aspect of the right arm. As pointed out by Head, herpes zoster only rarely involves the upper limbs.

Secondly, several reports have been published of the appearance of herpes zoster over the distribution of referred pain in other diseased conditions. Moreover, pain was an outstanding feature in all these, viz. biliary colic, renal colic, abdominal colic, pleurisy, pericarditis, appendicitis, and arthritis. Curtain (1902) has observed the appearance of herpetic eruptions over an acute arthritic knee joint, over the area of pain and friction in a dry pleurisy, over an area of localized peritonitis, and over the left kidney during a bout of hæmaturia. Bittorf (1911), Rosenbaum (1911), Kanera (1911), Rosenberg (1911), and Krotoszymer (1911) have described instances of the appearance of herpes zoster over the homolateral segments, Th. 10 or Th. 10 and 11, in cases of renal colic due to calculus or intermittent hydronephrosis. Severin (1926) observed two similar cases and one in which the herpes rash appeared over segment Th. 9 on the right side in a case of gallstone colic. In patients suffering from gastric colic with hypermotility of the stomach observed by fluoroscopy, Hess and Faltitschek (1925) described the appearance of herpes zoster over the lower thoracic segments. The gastric disturbances disappeared with the subsidence of the eruption. Lastly, Loeper and Loisel (1937) reported the occurrence of herpes zoster over the area of referred pain (C. 4, Th. 1 and 2) in acute rheumatic pericarditis. On the ninth day of an attack of acute rheumatism their patient, who was suffering from pericarditis, with a friction rub, developed an herpetic eruption, which disappeared with the exhibition of salicylates and the subsidence of the pericarditis.

The crises of pain in *tabes dorsalis* are sometimes attended by the develop-

ment of herpes zoster. In recurrent gastric crises the zoster may make its appearance along the costal margin (Udaondo, 1928 ; Laignel-Lavastine and Boquien, 1932) and may appear over the legs following paroxysms of lightning pains. The known involvement of the root ganglia in this disease probably accounts for such phenomena, and may have been the reason for the outbreak of herpes zoster in our example with a syphilitic aneurysm (Case 10).

Thirdly, our contention gains support when it is recalled that other skin lesions have been observed along the line of radiation of pain in angina pectoris. Mackenzie (1893) recorded a case in which, following a series of rapidly recurring anginal attacks with radiation of pain down the left arm, a streak of ecchymoses, six inches in length, developed on the left arm without obvious cause, and was assumed to be trophic. That such a lesion probably resulted from disturbance in the thoracic posterior root ganglia is suggested by the known occurrence of similar ecchymotic areas along the path of the lightning pains of *tabes dorsalis* ; in the latter condition we know these ganglia are involved. Allbutt (1915) quoted two patients described by Gasne and Chiray (1905) ; both suffered from typical angina pectoris and both developed a peculiar rash resembling lichen planus along the areas of referred pain. In both it spread along the ulnar aspects of arm and forearm, and in one it involved the left chest wall also.

Admitting for the moment, then, that the appearance of the herpes zoster is in some way related to the second pathological condition present, viz. ; disease of the coronary arteries, we may consider by what possible mechanism this can be brought about. Herpes zoster may be due to invasion of the posterior root ganglia by a specific virus, and involvement of the ganglia by adjacent disease processes can produce the condition. Leucæmic infiltration, Hodgkin's disease, tumours, and syphilis may act in such a manner. It is perhaps not widely known, however, that there is evidence that it may result in a reflex manner following repeated irritation of the ganglia by impulses from a diseased viscus. Head and Campbell (1900) wrote "the trophic disturbance of the skin is an extreme form of activity of the same cells, disturbance of which by afferent impulses along the white ramus produces the hyperalgesia that accompanies visceral and referred pain. . . . The eruption is due to intense irritation of cells in the ganglion which normally subserve the function of pain, and more particularly that form of pain produced by afferent visceral impulses. . . . Some ganglia seem more prone to attack than others. . . . the ganglia most commonly affected are those which receive afferent impulses from the viscera."

Gaule (1894) was among the first to produce trophic changes in the skin of experimental animals by stimulation of the ganglia. He especially noted that these trophic effects were by no means confined to the segment served by the stimulated ganglion, but spread to the opposite side and over the whole body. This is of interest in view of our findings in some cases that the herpes may appear in adjacent segments, or even, as in Case 6, on the opposite side.

Krogh (1924) during his investigations on the physiology of human capillaries wrote "In herpes zoster we have evidence that a large number of capillaries

... are in direct connection with posterior root fibres and become dilated when these are stimulated . . . by pathological processes."

Lewis and Marvin (1927), in like vein, concluded that the probable explanation for herpes zoster was that antidromic impulses released a histamine-like substance in the skin area of that segment, with capillary dilatation and blister formation. They suggested the mechanism was thus a modified triple response ; the period of stimulation is prolonged and the wheal is replaced by a blister.

For these reasons, then—the repeated clinical observation of herpes zoster in anginal patients, the analogy of the herpetic eruption in other painful visceral states, the occurrence of other skin lesions along the line of radiation of anginal pain, and the existence of an anatomical nervous pathway between ganglion and skin that can conduct antidromic impulses—it is reasonable to conclude that the appearance of herpes zoster over the area of referred pain in anginal patients is not fortuitous. It signifies the repeated bombardment of spinal root ganglia of the thoracic cord by afferent impulses from the diseased heart.

SUMMARY AND CONCLUSIONS

We have described twelve instances of the occurrence of herpes zoster in anginal subjects. In ten of these the zoster appeared after the anginal attacks had become established. In two the zoster first appeared about two years before the first anginal paroxysm. In both these, as in the former group, a close association was apparent between the distribution of the herpetic eruption and that of the anginal pain.

Attention has been drawn to the occurrence of herpes zoster over the area of referred pain from other diseased viscera also, viz., the pleura, pericardium, gall bladder, kidneys, stomach, and appendix. We have suggested that repeated bombardment of spinal root ganglia by afferent impulses from the ischæmic heart gives rise to antidromic impulses that lead to vasodilatation and blister formation in referred cutaneous areas. The herpetic eruption is thus a trophic manifestation of disease of the coronary vessels in these cases.

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SEX AND AGE FACTORS IN ACUTE AND CHRONIC VALVULAR DISEASE

BY

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In a pathological study of cardiac disease in pregnancy, controls were needed from women of child-bearing age who were not pregnant. This raised the question of the influence of the sex or age of patients on the various aspects of valvular disease. It is, however, difficult to get satisfactory pathological information on this point. Clinical studies of these factors have been made by Gillespie (1898), Andrew (1909), MacDonald (1914), and Willius (1926); some pathological details are included, but they are inadequate for the present purpose. The accuracy of clinical diagnosis of chronic valve lesions is a little over 50 per cent., as shown by Cabot (1926) and Frey (1936), so that the information from clinical studies about the sex and age differences of the valve lesions is not sufficiently reliable. There are certain relevant pathological data in the papers of Cabot (1914 and 1926), Coombs (1924), and Cowan and Ritchie (1935), which are discussed later, but much of the information we required is not given by these authors.

An analysis was therefore made of the records of 11,700 consecutive autopsies in two large general hospitals and one children's hospital in Glasgow, the numbers of males and females being approximately equal. In these cases clinical and pathological details were abstracted of the 1057 patients that showed post mortem any chronic or acute valve lesions, excluding minor senile changes in the aortic valve. The few patients in these general hospitals who died during pregnancy or within eight weeks of delivery are excluded from this control series.

No investigation has been made of the microscopic appearances of the valves or heart muscle, so this limits the scope of our figures to lesions which are obvious to the naked eye. Certain of the pathological and clinical records may be incomplete, but this source of potential error appears insufficient to vitiate the general conclusions. No attempt has been made to assess the severity of the mechanical defects of the valve, a severe mitral stenosis and an incompetence due to minor scarring both being classed as chronic mitral lesions.

* Working with the aid of the Medical Research Council and the Robert Jardine Research Scholarship.

The valve lesions are considered under the headings of :

I. Chronic valve lesions, i.e. scarring of valves that is apparently of rheumatic type.

II. Recurrent endocarditis, i.e. simple acute vegetations on old scarred valves or on valves that were previously healthy in a heart with old chronic valvular disease.

III. Simple acute endocarditis, i.e. vegetations of rheumatic type in a heart without recognizable chronic lesions.

IV. Ulcerative or subacute bacterial endocarditis, whether on previously damaged valves or not.

V. Lesions of the aortic valve, either syphilitic or of the senile variety classed as primary sclerosis.

I. CHRONIC VALVE LESIONS

Excluding aortic lesions due to senile sclerosis or syphilis, 629 patients had scarring of one or more valves, producing stenosis or incompetence, and of the type usually accepted as due to old rheumatic involvement. Often there was a superadded simple acute or ulcerative endocarditis ; these will be discussed later.

The incidence of chronic rheumatic valvular disease was much higher in adults than in children. There were 596 cases in 7000 necropsies on patients aged 12 and over (8.5 per cent.), but only 33 out of 4700 in children under 12 (0.7 per cent.). These figures are slightly higher than those of Davis and Weiss (1932), who found 222 out of 3951 necropsies on patients 10 years old and over (5.6 per cent.) and only 4 out of 821 in children under 10 (0.5 per cent.).

SEX AND AGE DIFFERENCES

The distribution of chronic lesions on the different valves has been studied by various authors (Edens, 1929), but no differentiation with regard to sex or age is found in their data, except in the work of Cabot (1926), who gives details of 208 patients.

In the present series the sex and age incidence of chronic lesions affecting (a) the mitral alone, (b) the aortic and mitral together, and (c) the aortic-mitral-tricuspid or the mitral-tricuspid, are plotted in Figs. 1 and 2 ; the number with each valve lesion being shown as a percentage of the total with any chronic valve lesion in the given age group and of that sex. The main points shown are the high relative incidence of aortic-mitral lesions in males, and of pure mitral lesions or of multiple valve lesions involving the tricuspid in females.

The number of cases is shown in Table I. From these it will be seen that the incidence of pure mitral and of mitral-tricuspid lesions is much greater in females than in males ; nearly three times up to the age of 25, and nearly twice over that age.

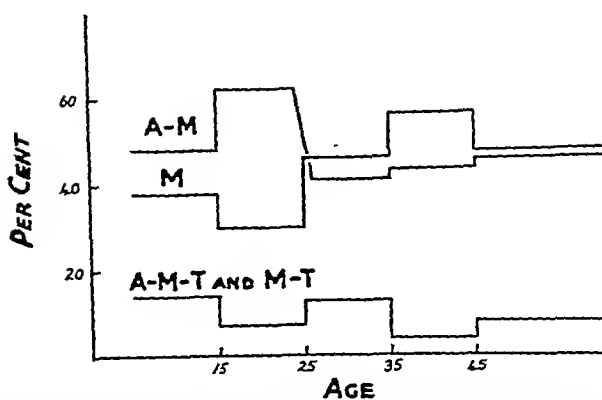


FIG. 1.—Percentage distribution of chronic valve lesions at different ages in males. M denotes mitral lesions; A-M, combined aortic and mitral lesions, etc.

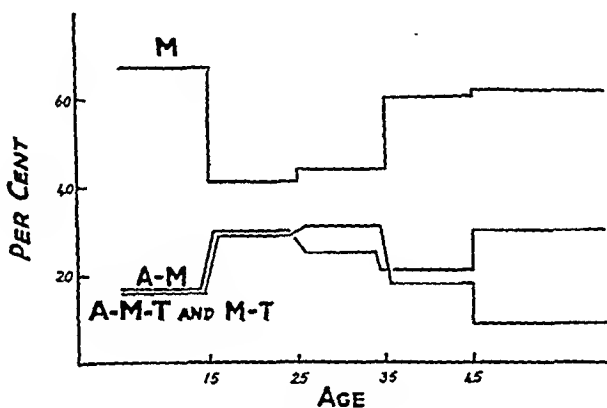


FIG. 2.—Percentage distribution of chronic valve lesions at different ages in females (see Fig 1).

TABLE I
SEX AND AGE INCIDENCE OF CHRONIC VALVE LESIONS

Sex	Age	M *	A-M	A-M-T	M-T	A	Others
Males ..	to 15	8	10	3	0	3	P-T
	16 to 25	9	19	1	1	3	P-T
	26 to 35	18	16	4	1	8	0
	36 to 45	26	21	1	1	12	0
	Over 45	44	45	5	3	16	A-M-P
	Total	105	111	14	6	42	3
Females ..	to 15	24	6	3	3	1	0
	16 to 25	18	13	7	6	3	0
	26 to 35	21	12	9	6	1	0
	36 to 45	41	14	7	6	5	M-T-P
	Over 45	84	41	8	4	4	0
	Total	188	86	34	25	14	1

* In this and all tables, M, A, T, and P stand for mitral, aortic, tricuspid and pulmonary valve lesions, and A-M, etc., for combined aortic and mitral lesions, etc.

On the other hand, a combined aortic-mitral lesion, including those with aortic-mitral-tricuspid involvement, shows the same absolute incidence in males and in females at every age group. The relative incidence is, however, higher in males.

The tricuspid is involved nearly three times as often in females as in males. A pure tricuspid lesion has not been observed ; it is more commonly associated with aortic-mitral than with mitral lesions. The two pulmonary-tricuspid lesions in young males were, as usually, associated with congenital heart disease.

Pure aortic lesions are rare in females but much commoner in males, particularly over 25, though some lesions in older males are open to the suspicion of being really due to primary sclerosis or syphilis.

Cabot (1926) noted the same predominance of mitral lesions in females and of aortic lesions in males. He found the aortic-mitral lesion more common in males than in females, but this is not striking in the present series if aortic-mitral-tricuspid is included with aortic-mitral disease.

AGE AT DEATH

The age at which patients die with various chronic valve lesions is about the same for pure mitral and for combined mitral and aortic lesions (Table I). On the other hand, patients with a tricuspid lesion superimposed tend to die much earlier, usually before the age of 35. The age of death with each valve lesion showed no essential difference between the sexes. Cabot (1926) considered that males tended to die earlier from mitral or combined lesions than females ; this does not agree with the present data.

MODE OF DEATH

This is of importance not only with regard to the chronic valve lesion, but also with regard to the incidence of recurrent endocarditis. Clinically the patients have been classified into the following six groups according to the manner of death.

Progressive Failure.—Patients with typical congestive heart failure, with the usual signs becoming gradually worse until death ; post mortem, chronic venous congestion of the lungs and abdominal viscera, and usually pulmonary infarcts ; no clinical or pathological evidence of any complicating disease.

Failure Combined with Other Illnesses.—Patients with typical congestive failure, combined with pathological evidence of some complicating disease. In some the major factor causing death was the failure, in others the intercurrent disease ; a few have been included that died of sudden heart failure, apparently without any gross congestion previously.

Acute Rheumatism or Chorea.—Patients with acute rheumatism or chorea at the time of death or during the previous six months. The expression "acute rheumatism" is used to indicate rheumatic fever, and does not include growing pains, sore throats, or tonsillitis. Many of the patients in this group died with clinical and pathological evidence of failure, but they are not included in the first two groups.

Intercurrent Illness.—Patients with no history or post-mortem evidence of failure, who died from other illnesses such as pneumonia or carcinoma, excluding rheumatism.

Sudden, Violent Death.—Patients that died suddenly as a result of street accident or suicide, nearly half of them before the age of 45. Apart from having old scarred valves, they appear to have been in normal health.

Ulcerative Endocarditis.—All patients with any chronic valve lesion in whom a superadded ulcerative endocarditis was found at death. Some died of failure, others of septicæmia or intercurrent disease; but all have been excluded from the previous groups.

RELATION OF VALVE LESIONS TO MODE OF DEATH

When the patients are considered according to the valves affected by the chronic lesion, there are certain striking differences in the mode of death. The actual numbers are shown in Table II. The chief points are the low incidence of failure in men with pure mitral lesions, the high incidence of failure in tricuspid lesions, and the high incidence of ulcerative endocarditis in chronic aortic lesions.

TABLE II
TYPE OF DEATH WITH EACH CHRONIC VALVE LESION

Sex	Type of Death	M	A-M	A-M-T and M-T	A
Males	Failure, simple and combined, and rheumatism	41	62	18	13
	Intercurrent disease and violence	56	33	1	14
	Ulcerative endocarditis	9	16	1	15
Females ..	Failure, simple and combined, and rheumatism	117	54	55	5
	Intercurrent disease and violence	56	25	3	5
	Ulcerative endocarditis	14	7	2	6

The more important age differences are that 80 per cent. of the deaths due to intercurrent disease without failure were in patients over 35, and that the ulcerative aortic lesions were commoner among the older men.

Cabot (1926) observed death from failure in only two thirds of his chronic tricuspid cases, which is less than in the present series, apparently because only one of his seven patients with mitral-tricuspid lesions had failure. In the present series there were 31 patients with mitral-tricuspid lesions, of whom 20 died of pure, and 6 of complicated failure.

II. RECURRENT ENDOCARDITIS

Of the 629 cases with chronic rheumatic valvular lesions, 71 had a superadded ulcerative endocarditis (see later). In the remaining 558, 244 had simple acute

vegetations, either on the scarred valves or, less frequently, on previously undamaged valves. This is referred to as recurrent endocarditis. This incidence of recurrent endocarditis in 46 per cent. of the chronic cases is in reasonable agreement with the findings of previous workers, whose combined data on 710 cases give an incidence of 40 per cent. : Gerhardt (1913), Coombs (1924), Cabot (1926), Clawson, Bell, and Hartzell (1926), Stone and Feil (1933), and Cowan and Ritchie (1935).

Pathologically the vegetations are indistinguishable from those of the various forms of simple acute endocarditis, and appear to have essentially the same ætiological factors. But they are much more liable to develop in a previously damaged heart than simple endocarditis in a normal one. This matter is well discussed by Gross and Friedberg (1936). It is difficult to form any good estimate of the age of the recurrent vegetations. Clinically they cannot be diagnosed during life except by inference, and generally are not recognized till after death. Histologically they are hyaline or fibrinoid masses of from 1 to 4 mm. in height, sometimes with, and sometimes without organization at their base ; while organization certainly indicates advancing age of the lesion, the rate at which it progresses in this situation is unknown.

CAUSE OF DEATH

The chief data on the incidence of recurrent endocarditis are shown in Table III, divided into sections according to the various clinical factors.

TABLE III

RELATIONSHIP OF RECURRENT ENDOCARDITIS TO AGE AND TO TYPE OF DEATH

Age	Progressive Failure		Failure Combined		Acute Rheumatism		Intercurrent Illness		Violent Death	
	Total Chronic	Recurr. End.	Total Chronic	Recurr. End.	Total Chronic	Recurr. End.	Total Chronic	Recurr. End.	Total Chronic	Recurr. End.
To 15	29	25	2	1	26	21	0	0	0	0
16 to 25	37	22	8	6	14	14	9	4	4	0
26 to 35	43	20	9	7	5	5	22	11	3	0
36 to 45	52	20	14	6	3	0	46	13	2	0
Over 45	87	36	33	11	2	1	98	20	10	1
Total	248	123	66	31	50	41	175	48	19	1

Progressive Failure.—Fifty per cent. of these cases had a recurrent endocarditis. This high incidence appears significant, though it is not clear whether the recurrence is due to the failure, or whether it indicates a carditis which caused the failure. Most patients before the final cardiac failure have temporary failure and recovery several times, when it seems probable that acute vegetations are frequently present. Davis and Weiss (1931) also noted the high incidence of acute vegetations in patients who died of failure, but they did not give figures. Gerhardt (1913) found recurrent endocarditis in 11 out of 23 cases with failure.

Failure combined with Other Illnesses.—Recurrent endocarditis was found in forty-seven per cent. of the cases, practically the same figure as in the pure failure group.

Acute Rheumatism or Chorea.—Eighty-two per cent. of the cases with acute rheumatism at the time of death or during the previous few months had recurrent lesions. But there are a certain number, particularly children, with no recurrent vegetations, though these are to be expected with active rheumatism. Karsner and Bayless (1934) in a study of hearts with Aschoff nodes found recurrent endocarditis in 39 of 51 cases with old valve lesions. The data given by Rothschild, Kugel, and Gross (1934), and by Werner (1936) with regard to the incidence of active infection of the heart in rheumatic fever cannot be compared with the present figures, as they did not deal with the incidence of acute endocarditis. Acute rheumatism is not usually fatal, and probably most cardiac patients who have subsequent attacks of acute rheumatism develop a recurrent endocarditis at these times.

Patients who gave a history of acute rheumatism many years previously did not show any striking incidence of recurrent endocarditis, when due regard was given to sex, age, and manner of death. This agrees with Frey (1936), who also points out that its incidence diminishes with the passage of time since the last attack of acute rheumatism.

Intercurrent Illnesses excluding Rheumatism.—Twenty-seven per cent. of these cases had a recurrent endocarditis. The intercurrent disease that caused death was often of a type such as pneumonia from which recovery is usual. Thus it appears probable that, during passing illnesses, many patients with old valvular disease develop a recurrent endocarditis which is not clinically recognized and heals later. There is no clear evidence as to whether this is due to a flare up of a quiescent rheumatic infection in the heart or to a new infection due to the intercurrent disease. These diseases were of the same types and were found in the same relative proportions in recurrent endocarditis as in simple acute endocarditis in patients with hearts previously normal, who had died of intercurrent disease. The outstanding difference was in the incidence of the acute vegetations; they were found in 27 per cent. of the patients who had old chronic valvular disease, and only in 1.5 per cent. of 10,643 patients with hearts previously normal.

The existence of this group is in itself sufficient evidence that a recurrent endocarditis does not always cause failure.

Sudden, Violent Death.—Among the 19 cases with chronic valve lesions in this group, the only one with recurrent endocarditis was an old man. These figures are small, but give no support to the theory that, in a person with an old valvular lesion but otherwise in good health, there may be frequent recurrent endocarditis without any exciting factor. This conclusion depends, of course, on the supposition that the vegetations are not rapidly evanescent.

EFFECT OF AGE AND SEX

Age.—Running right across these clinical factors is the great variation due to the age of the patient. The percentage of patients in each age group who

TABLE IV
RECURRENT ENDOCARDITIS AT VARIOUS AGES

Age			Total Chronic Valve Lesions	Recurrent Endocarditis	Percentage
4 to 7	17	15	88
8 to 11	16	13	81
12 to 15	25	19	76
16 to 25	71	46	65
26 to 35	81	43	53
36 to 45	118	39	33
Over 45	230	69	30

showed recurrent lesions is given in Table IV. These are very close to the percentages given by Coombs (1924) from a study of 98 necropsies; his figures, which appear to be the only ones published, range from 88 per cent. under 10 years to 24 per cent. over 40 years of age. The high incidence of acute rheumatism and of death from progressive failure is probably responsible for the height of the figures in the earlier age groups, but there appears to be a true diminution in the incidence of recurrent endocarditis in older patients, quite apart from this. When the patients in each clinical group are considered separately, as in Table III, a similar steady reduction of the incidence of recurrent endocarditis with advancing age is obvious.

Sex.—There were 93 cases among 240 male patients with chronic valve lesions, and 151 cases among 318 females. It is, however, not satisfactory to compare the gross incidence of recurrent endocarditis in males with that in females without regard to the significant factors; the high incidence of acute rheumatism and of failure in females distorts the picture. When the cases are grouped on a clinical basis there is no obvious difference between the sexes except in the deaths from progressive failure (Table V). In this condition the incidence of recurrent endocarditis falls suddenly at about 15 years of age in

TABLE V
SEX DIFFERENCES OF RECURRENT ENDOCARDITIS IN DECOMPENSATION

Age	Males			Females		
	Total Chronic	Recurrent Endocarditis	Percentage	Total Chronic	Recurrent Endocarditis	Percentage
To 15 ..	10	9	90	19	16	84
16 to 25 ..	15	6	40	22	16	73
26 to 35 ..	20	6	30	23	14	61
36 to 45 ..	21	8	38	31	12	39
Over 45 ..	25	7	28	62	29	47

males, but not until about 35 in females. This sex difference is significant for the original purpose of this study, the provision of control figures for the investigation of cardiac disease in pregnancy.

VALVES AFFECTED

The valves affected by the acute recurrent vegetations are shown in Table VI, grouped according to the previous chronic valve lesion ; the figures show the actual number of cases with each lesion.

TABLE VI
VALVES AFFECTED BY RECURRENT ENDOCARDITIS
MALES

Recurrent Endocarditis				Chronic Valve Lesion					
				M	A-M	A-M-T	M-T	A	Others
None	63	53	7	3	20	P-T
M	21	11	2	1	0	A-M-P
A-M	4	23	2	0	0	0
A-M-T	5	3	1	0	3	0
M-T	0	0	1	1	0	0
A	3	3	1	0	4	0
Others	A-P	T, A-T	0	0	0	0

FEMALES

Recurrent Endocarditis				Chronic Valve Lesion					
				M	A-M	A-M-T	M-T	A	Others
None	97	35	15	15	4	M-T-P
M	43	11	3	2	2	0
A-M	13	21	3	0	1	0
A-M-T	3	4	3	0	0	0
M-T	2	0	1	1	0	0
A	11	7	6	1	1	0
Others	A-M-P-T, A-T, A-M-P, A-M-P	A-T	T, A-T	T, T, T A-T, T-P,	0	0

Previously Fibrosed Valves.—Recurrence occurred on 36 per cent. of the 522 fibrosed mitral valves, on 35 per cent. of the 257 fibrosed aortic valves, and on 19 per cent. of the 79 fibrosed tricuspid valves. This rough proportion of 2 : 2 : 1 in the incidence of recurrence on mitral : aortic : tricuspid holds good for any subdivision of the cases according to sex, age, or mode of death, though the actual percentages are influenced by these factors. This relative immunity

of the tricuspid to recurrent endocarditis may be connected with the relative immunity of this valve to endocarditis in general.

These findings have a bearing on the question of recurrence on chronic lesions of multiple valves. In chronic aortic-mitral lesions the recurrence affects both fibrosed valves more frequently than one. In chronic mitral-tricuspid and aortic-mitral-tricuspid lesions recurrence on three or even two valves is much less frequent than recurrence on either valve separately.

Spread to Fresh Valves.—If there are fibrosed valves in a heart, the other healthy valves show a great tendency to develop an acute endocarditis, as compared with a heart in which none of the valves have been scarred (see Table VII). The valve incidence of this spreading endocarditis is about 3 : 3 : 1 for mitral : aortic : tricuspid, which is very similar to the 2 : 2 : 1 figure for recurrence on scarred valves. This proportion holds in all the clinical subdivisions. Generally this spread to fresh valves is associated with recurrent endocarditis on one or more of the scarred valves—46 of the 255 cases where there was a recurrent endocarditis. Occasionally, however, the acute endocarditis affects normal valves without any recurrence on the fibrosed valves—19 cases, 15 of which were women ; here the acute endocarditis affected only the aortic, and the fibrosed mitral or tricuspid had no recurrent lesions.

TABLE VII
RECURRENT ENDOCARDITIS SPREADING TO NEW VALVES

Non-scarred Valve	Hearts with Previously Damaged Valves			Hearts Previously Normal		
	Total	Spreading Endocarditis	Percentage	Total	Simple Acute Endocarditis	Percentage
Mitral ..	36	6	16.6	10,643	126	1.2
Aortic ..	301	46	15.3	10,643	82	0.8
Tricuspid..	479	25	5.2	10,643	12	0.1

Age and Sex Incidence.—A spread to new valves occurs most frequently with a pure chronic mitral lesion, as these patients have, of course, more unaffected valves than patients with multiple old lesions (a chronic aortic lesion of rheumatic type is relatively uncommon). Thus, as shown in Table VI, the spread is absolutely more frequent in females, in view of the higher number of pure chronic mitral lesions in that sex. When, however, the incidence is considered in relation to the number of cases in which spread was possible, there does not appear to be any significant sex difference in the valves affected. The age factor is much the same as in recurrent endocarditis, there being a gradual decrease in the proportionate incidence with advancing age.

The spreading lesion shows a relationship to the type of death similar to that of recurrent endocarditis in general ; it occurs in about one-third of the patients dying of acute rheumatism or of failure and in about one-seventh of the patients dying of intercurrent diseases.

III. SIMPLE ACUTE ENDOCARDITIS

Simple acute endocarditis is used here to mean any vegetations which are not obviously ulcerative or subacute bacterial, and where there is no chronic valve lesion macroscopically recognizable. As in recurrent endocarditis, the vegetations are small hyaline or fibrinoid masses about 1 to 4 mm. in height. It seems probable that they can develop in a few days, since they are sometimes found after quite short illnesses. A differentiation of these vegetations into rheumatic, as opposed to non-bacterial thrombotic or terminal, is made by some authors on the basis of the size and exuberance of the vegetations, as well as on the histology. While the non-rheumatic vegetations are sometimes large, the vegetations of all types are presumably small in the early stages, so no attempt has been made to subdivide the group on pathological appearances ; any subdivision here has been made on clinical grounds alone.

Though cases of ulcerative endocarditis have been excluded from this group, a few classified as simple acute endocarditis may really have been the early stages of the former. The difficulty of naked eye diagnosis is illustrated where there is a gross ulcerative endocarditis on one valve and also apparently simple vegetations on the same valve or on others. The co-existence of simple and ulcerative endocarditis on the same valve and the difficulty of differentiating them in the early stages by naked eye are discussed by Clawson and Bell (1926) and by Von Glahn and Pappenheimer (1935).

The numbers in the present series showing simple acute endocarditis are shown in Table VIII ; its rarity in children under 3 is referred to by Norris (1911) and de Vecchi (1931).

TABLE VIII
AGE INCIDENCE OF ACUTE ENDOCARDITIS

Age	Cases with Acute Endocarditis
To 3	4
4 to 7	14
8 to 11	14
12 to 15	11
16 to 25	15
26 to 35	13
36 to 45	23
Over 45	66

ÆTIOLOGY

The clinical conditions at or shortly before death are given in Table IX ; they are similar to those found with recurrent endocarditis in patients that die without failure.

Acute rheumatism or chorea is most frequently found in the young, and among these it is almost twice as common in females as in males.

The miscellaneous group includes pyogenic infections such as pneumonia, meningitis, and burns, and a variety of conditions such as toxic goitre and tuberculosis ; a history of acute rheumatism or chorea was not obtained in any

of these. Apart from a high incidence in young girls, there is no obvious sex difference. This group also includes three surprising cases, patients who were killed accidentally, and post mortem were found to have small vegetations on the aortic or mitral; two were young adults. It is not possible to say whether there had been any minor illnesses, such as tonsillitis, before the fatal accident.

The remaining group of uræmia, hypertension, and carcinoma naturally provides most of the cases in later life. This type is usually referred to as terminal, and it is unlikely that any of these could have recovered. There is no obvious sex difference.

TABLE IX
ÆTIOLOGY OF ACUTE ENDOCARDITIS

Ætiological Factor	Sex	Age					
		To 15	16-25	26-35	36-45	Over 45	Total
Acute rheumatism or chorea	Male	11	1	0	1	1	14
	Female	15	3	1	1	2	22
Miscellaneous ..	Male	4	4	5	2	17	32
	Female	13	3	5	6	14	41
Uræmia, hypertension, or carcinoma	Male	0	2	1	4	19	26
	Female	0	2	1	9	13	25

VALVES AFFECTED

There is no difference between the valves affected by chorea and those affected by rheumatism: see Table X, where they are grouped according to

TABLE X
VALVES AFFECTED BY ACUTE ENDOCARDITIS

				Sex	M	A-M	A-M-T or M-T	A
<i>To age 15</i>								
Rheumatism	Male				3	4	4	0
	Female				5	9	1	0
Miscellaneous	Male				2	2	0	0
	Female				9	3	1	0
<i>Over age 15</i>								
Rheumatism	Male				0	2	1	0
	Female				3	3	1	0
Miscellaneous	Male				15	4	0	8
	Female				12	3	3	8
Uræmia, hypertension, or carcinoma	Male				7	6	1	12
	Female				18	2	0	5

ætiological factors. In children, most of the acute endocarditis is due to rheumatism, with the striking exception of pure mitral lesions in girls, which are more frequently *not* associated with rheumatism. Below the age of 15 rheumatism never causes an acute aortic lesion alone in either sex, but frequently an acute aortic-mitral lesion, particularly in girls. Over the age of 15, most of the acute endocarditis is not rheumatic in origin. After 35 there is a striking increase of pure mitral lesions, mainly in women, and also of pure aortic lesions, mainly in men.

IV. ULCERATIVE AND SUBACUTE ENDOCARDITIS

The term "ulcerative endocarditis" is used to cover not only the true ulcerative or malignant lesions but also subacute bacterial endocarditis of *Streptococcus viridans* type. The subject is well reviewed by Blumer (1923), Horder (1926), Thayer (1926), and Segal (1936). Though early ulcerative endocarditis may be hard to distinguish macroscopically from simple endocarditis, the fully developed, large, friable vegetations are quite characteristic. The cases included as subacute bacterial endocarditis are classified as occurring on previously damaged valves. They are selected on a pathological basis and not on the criterion adopted by Clawson, Bell, and Hartzell (1926) of a clinical history of over six weeks. This difference may account for the very high incidence of subacute endocarditis in certain American clinics, e.g. 60 per cent. of all hearts in which there was any valve lesion (Clawson, 1924).

It is not clear how often the ulcerative lesion begins as such or how often as a further development on previously simple acute vegetations; there is a considerable weight of evidence that it may develop on simple recurrent endocarditis, as has been shown by Von Glahn and Pappenheimer (1935). It is of interest in this connection to note the great frequency of joint pains in the very early stages of the illness, without any septic arthritis, and before any recognizable embolic phenomena have developed.

DEVELOPING ON VALVES PREVIOUSLY NORMAL

Primary ulcerative endocarditis is relatively uncommon in children up to 11; in the present series there were 9 out of 4700 autopsies (0·2 per cent.), whereas over that age it was found 89 times in 7000 autopsies (1·3 per cent.). In adults the main point of interest is the biphasic incidence—very frequent up to 25, and then later, over 45. The cases in youth or early middle age were all septicæmic in origin or clinical course: over 45, about half were of septicæmic type, but the others were incidental findings post mortem in patients dying from other diseases—carcinoma of stomach, 8 cases; other carcinomas, mainly of biliary tract, 5 cases; uræmia due to prostatic enlargement or renal calculi, 6 cases; miscellaneous conditions, 4 cases.

There is a slightly higher incidence in males than in females, related to differences in the valves affected: pure aortic lesions affected males almost exclusively; the mitral was involved alone about twice as often as the com-

bined aortic-mitral; the pulmonary, which was hardly ever the site of simple endocarditis, was sometimes affected by the ulcerative lesion, particularly when there was a congenital basis or a spread to all the valves. None of the present cases appeared to be related to clinical gonorrhœa. There is no obvious valve difference between the septicæmic and the non-septic types. The numbers showing each valve lesion are grouped in Table XI according to sex and age. Some of the older patients may have had early senile changes in the aortic valve, which predisposed them to an ulcerative lesion, but this does not explain the high incidence of mitral lesions in the older men.

TABLE XI
ULCERATIVE ENDOCARDITIS ON NORMAL VALVES

	Age	M	A-M	A-M-T	A	Others	Total
Males ..	To 15	5	0	0	2	A-M-P-T; P	9
	16 to 25	5	2	1	5	P	14
	26 to 35	2	1	0	1	M-T-P	5
	36 to 45	0	1	0	5	0	6
	Over 45	14	5	1	4	A-T	25
Females ..	To 15	5	3	0	0	0	8
	16 to 25	4	5	0	0	A-T; P	11
	26 to 35	4	0	0	0	M-T	5
	36 to 45	2	0	0	0	0	2
	Over 45	4	5	1	2	T	13

DEVELOPING ON PREVIOUSLY DAMAGED VALVES

In 42 per cent. of the 169 cases with ulcerative endocarditis a pre-existing chronic valve lesion was recognized, and possibly in some others the ulcerative endocarditis had destroyed any evidence of previous scarring. The frequency with which previously scarred valves are affected by ulcerative endocarditis is greater in males than females; 17 per cent. of 240 males and 9 per cent. of 318 females. A similar sex incidence was noted by Davis and Weiss (1931); 20 per cent. of 272 males and 10 per cent. of 213 females. When the sexes are not differentiated an intermediate figure is found; 12 per cent. of 348 patients with previously scarred valves in the combined series of Stone and Feil (1933), Frey (1936), and Epstein and Schwedel (1938).

Table XII shows that in males the incidence rose sharply at about 25, i.e.

TABLE XII
AGE AND SEX INCIDENCE OF ULCERATIVE ENDOCARDITIS ON SCARRED VALVES

Age Group			Males	Females
To 15	3	1
16 to 25	4	6
26 to 35	12	3
36 to 45	11	6
Over 45	12	13

the age when the fall occurs in the number with hearts previously normal: in females the incidence was relatively low except in people over 45. All but 5 of the 25 cases over 45 were septicæmic in type.

The numbers with each individual valve lesion are shown in Table XIII. In more than a quarter there was a spread of the ulcerative lesion to valves that had previously been undamaged. The frequency with which any chronic rheumatic valve lesion was affected by ulcerative endocarditis is also shown in this table. Ulcerative endocarditis affects about 36 per cent. of patients that have a pure chronic aortic lesion of rheumatic type, and this holds good when the cases are analysed according to sex or age; it is the same in young women as in older men, though, of course, the absolute numbers of chronic aortic lesions are much higher in the male group. In chronic mitral or aortic-mitral lesions ulcerative endocarditis occurs in about 10 per cent. of cases, again without any significant sex or age differences. The low incidence of ulcerative endocarditis on the aortic in chronic aortic-mitral lesions, as compared with its higher incidence in chronic aortic lesions without fibrosis of the mitral, is of interest. White (1937) has suggested that there is a relationship between the degree of stenosis of the mitral and the tendency for ulcerative endocarditis to affect this valve, but we have not investigated this. In contrast to the other valves, patients with chronic tricuspid lesions show a very low susceptibility to ulcerative endocarditis, only about 4 per cent.; the total incidence is actually less than that of ulcerative endocarditis on the tricuspid in patients with no chronic lesion of this valve. This may be because patients with chronic tricuspid lesions die earlier in life. Libman (1923) has shown that ulcerative endocarditis is relatively common on the tricuspid, as compared with subacute bacterial endocarditis. His total figures of 16 tricuspid involvements out of 156 cases of ulcerative and subacute bacterial endocarditis are in reasonable agreement with the present figures: 12 tricuspid involvements out of 169 cases of ulcerative or subacute bacterial endocarditis, with or without a previous chronic lesion.

TABLE XIII
ULCERATIVE ENDOCARDITIS ON SCARRED VALVES

Ulcerative Endocarditis				Chronic Valve Lesions					
				M	A-M	A-M-T	M-T	A	Others
None		270	174	47	29	37	3
M	14	4	1	1	0	0
A-M	5	13	0	1	8	0
A-M-T	2	0	0	0	1	0
M-T	1	0	0	0	0	0
A	1	6	0	0	11	0
Others	0	0	0	0	A-T	P-T (cong.)

V. PRIMARY AORTIC SCLEROSIS AND SYPHILIS

Lesions of the aortic valve due to syphilis or primary sclerosis are only important in the present study because they have to be differentiated from the

rheumatic lesions ; only exceptionally does this provide any difficulty. The two conditions were nearly all found in patients over 45, though syphilitic cases were sometimes seen in the previous decade. After excluding all minor senile changes, the actual numbers were as follows—primary sclerosis : males 58, females 17 ; syphilis : males 82, females 14.

Small vegetations due to a superimposed acute endocarditis were present in four of the syphilitic and in eight of the sclerosis cases. This appears to be a chance complication, the incidence being roughly similar in the syphilitic patients and in those with otherwise normal hearts dying in the same age periods. The slightly higher incidence among the sclerosis cases is probably spurious, depending on the initial exclusion of many cases with minor thickening of the aortic, but without any acute vegetations. Gerhardt (1913) found a recurrent endocarditis in two out of eleven arteriosclerotic valves.

DISCUSSION

It is accepted pathologically that vegetations on a valve are frequently an indication of an acute valvulitis which may go on to scarring later. This applies particularly to acute rheumatism. On the other hand, it is impossible to say what might have occurred subsequently, if a patient with advanced carcinoma could have recovered after having developed a terminal endocarditis. There is, however, a large group, intermediate between acute rheumatism and terminal endocarditis, that includes not only simple endocarditis but also endocarditis recurring or spreading to other valves. Though, of course, all the patients in this intermediate group had died, most of them were suffering from diseases not necessarily fatal ; it is in these that the subsequent fate of the valve is in doubt.

These hearts do not have the microscopic changes in the myocardium that characterize acute rheumatism, but this cannot be accepted as proof that scarring of the valve will not occur. The mere occurrence of the vegetations suggests co-existing acute valvulitis that could be the basis of subsequent fibrosis. If such scarring occurred on a previously normal valve, it would provide a reasonable explanation for a number of the cases of chronic valvular disease that originate in patients with no ascertainable history of acute rheumatism ; if it developed from a recurrent endocarditis on a previously scarred valve, the mechanical lesion would be aggravated. There is also the complementary question of how often cases of acute valvulitis that leads to subsequent scarring of the valves may run their course without ever developing any vegetations on the valves. This is an important problem in children, as has been shown by de Vecchi (1931).

The significance of recurrent endocarditis is especially doubtful. Is it (a) a terminal condition, or (b) an occasional development in the presence of certain exciting factors, or (c) an intermittent process coming and going unsuspected for many years after the original heart lesion, without any particular causation apart from the continued and symptomless presence of the aetiological agent of rheumatism, or (d) a serious complication of chronic valvular lesions

that commonly causes death from the associated myocardial damage (Cowan and Ritchie, 1935) ?

A study of the present kind might have given some answer to these questions in view of the marked differences in the valves affected by acute or chronic lesions at different ages and in different sexes. There are, however, many difficulties in attempting any correlation. Account must be taken of four factors which may play a part in the distribution of the various types of valve lesions at different ages. First, the age at the onset, which is only known in a certain number. Secondly, the progress of the lesion ; if the case starts early, it seems more likely that it will progress on the affected valve and also spread to new valves than if it starts in later life ; this presumption is based on the age incidence of recurrent endocarditis. Thirdly, the age at which the valve lesion causes death, e.g. patients with a tricuspid lesion usually die earlier than patients who have not. Fourthly, a factor that has not been discussed, the severity of the individual valve lesion. It is, therefore, not possible to assume that the patients dying in any age group provide a representative sample of the cardiac population at that age. Nevertheless the group of children up to the age of 15 is probably subject to the least complications, and may be used for an attempt to find some correlation between acute or recurrent endocarditis on the one hand and chronic valve lesions on the other. The fundamental problem is how frequently chronic valve lesions are the sequel of acute endocarditis or are aggravated by a recurrent endocarditis. Such a recurrent endocarditis might be assumed for purposes of discussion to develop occasionally at intervals during the patient's life, as a result of temporary failure or intercurrent illness, and to have the same incidence on previously scarred valves or spreading to normal valves as is found post mortem.

Mitral and Aortic-Mitral Lesions in Childhood.—First the ratio of lesions affecting only the mitral to lesions affecting the aortic and mitral together. In girls up to 15, acute endocarditis without previous valve lesions involves both valves together just as frequently as the mitral alone. But during this age period in girls a chronic lesion affects the mitral alone three times as frequently as the aortic and mitral together. No satisfactory explanation for this preponderance of the pure chronic mitral lesion in girls can be given from a study of the acute endocarditis. On the other hand, in boys up to 15 the correlation is good ; the aortic and mitral are affected together very slightly more frequently than the mitral alone, both by simple endocarditis and by chronic lesions.

Mitral and Aortic-Mitral Lesions in Young Adults.—In girls up to 15 about one third of the patients with chronic mitral lesions have post mortem a spread of acute endocarditis to the aortic. Any fibrosis following these new vegetations ought to lead to an increase of chronic aortic-mitral lesions at the expense of chronic mitral lesions in the next decade. This is the case ; there are rather more chronic aortic-mitral lesions than mitral lesions post mortem in females between the ages of 16 and 25, in contrast to the findings in young girls. In boys up to 15 there are relatively few pure chronic mitral lesions and less than one fifth of these have spread to the aortic. Theoretically this should only cause

a slight increase in the ratio of chronic aortic-mitral to chronic mitral lesions in the next decade : this is again the case.

Tricuspid Lesions.—There is thus some suggestion that these spreading vegetations do lead to subsequent fibrosis in the case of the aortic. But when the tricuspid is under consideration this view completely fails to explain the facts : taking the figures for all ages ; (a) the incidence of simple acute endocarditis on this valve was identical in both sexes, 6 males and 6 females ; (b) in the presence of other chronic valve lesions, spread of acute vegetations to this valve was also the same in both sexes, 12 males and 12 females ; but (c) the incidence of chronic tricuspid lesions was about three times as high in females as in males, 60 females and 22 males.

In view of these difficulties even in young subjects, no attempt will be made here to explain the increasing incidence of chronic mitral lesions relative to other chronic valve lesions in older women.

RHEUMATIC LESIONS

In Childhood.—The relation of the valve lesion to a history of rheumatism also presents difficulties. The preliminary consideration may be restricted to children up to 15 (Table XIV). In boys the proportion with acute endo-

TABLE XIV
RELATIONSHIP OF RHEUMATISM TO VALVE LESIONS IN CHILDHOOD

Sex	Valve	Cases of Acute Endocarditis	Acute Rheumatism at Death	Chronic Valve Lesions	History of Rheumatism
Males under 15 ..	M	5	3	8	5
	A-M	6	4	10	8
	A-M-T or M-T	4	4	3	2
	Total	15	11	21	15
Females under 15 ..	M	14	5	24	18
	A-M	12	9	6	5
	A-M-T or M-T	2	1	6	4
	Total	28	15	36	27

carditis of any particular valve or valves and acute rheumatism in the few weeks before death is much the same as the proportion with a corresponding chronic lesion and acute rheumatism some years before. In girls this holds good for lesions of combined valves. But there is a striking difference with pure mitral lesions, where, though three-quarters of the chronic lesions have a history of rheumatism, as with other valves and in boys, only about one-third of the cases of acute endocarditis are related to rheumatism. The figures are small, but the difference seems significant.

The other contrast is as follows. In acute endocarditis due to rheumatism in boys or in girls, the mitral is affected alone in about one-third of the cases and the other two-thirds show multiple valve lesions. In chronic valve lesions following rheumatism this also holds good in boys, the mitral being affected alone in about one-third. In girls, on the other hand, such lesions affect the mitral alone in two-thirds and only one-third are multiple valve lesions.

Subsequent Fate.—Theoretically, the longer the patient lives after the original valve lesion, the more he will be exposed to attacks of recurrent or spreading endocarditis; and, if these lead to fibrosis, the greater the liability to multiple chronic valve lesions. But, when the cases of heart disease dating from acute rheumatism are studied with regard to the duration of life after the onset of the heart lesion, there is no evidence of any development of chronic lesions on fresh valves with the passage of time. The valve distribution shows the same sex differences, whether the rheumatism dates from early in life or later, and whatever the duration of life since the first attack of rheumatism. Table XV shows the

TABLE XV
CHRONIC VALVE LESIONS FOLLOWING RHEUMATISM

Sex	Chronic Valve Lesion	Acute Rheumatism before 15		Acute Rheumatism after 15	
		Death within 10 Years	Death over 10 Years later	Death within 10 Years	Death over 10 Years later
Males	M	5	4	3	4
	A-M	8	10	9	10
	A-M-T or M-T	2	3	0	1
	A	0	1	1	2
Females	M	18	15	12	12
	A-M	5	6	5	4
	A-M-T or M-T	4	2	3	7
	A	0	0	1	0

valve distribution of the chronic lesions of 157 cases in which the date of the first attack of rheumatism was known. The valve incidence of the chronic lesions that date from rheumatism is almost the same throughout life when each sex is considered separately. On the other hand, as has been shown earlier, there are quite marked age differences when the chronic lesions are considered as a whole, i.e. those following acute rheumatism and those without any such history. This raises the possibility that the cases following rheumatism may have a completely different valve distribution at various ages from those not following rheumatism. Taking all the chronic valve lesions of Table I the percentages in which a history of acute rheumatism was obtained are shown in Table XVI. The general fall with advancing age is probably partly due to a failure of memory by the patient, but this explanation will not account satisfactorily for the strikingly low figures in the case of pure mitral lesions in males over 15 years of age.

TABLE XVI
PERCENTAGE OF CHRONIC LESIONS WITH PREVIOUS RHEUMATISM

Age Group	Males				Females			
	M	A-M	A-M-T or M-T	A	M	A-M	AM-T- or M-T	A
To 15	63	80	66	0	75	83	66	0
16 to 35 ..	3	54	86	18	46	56	46	25
Over 35 ..	9	27	20	4	29	31	44	0

Consideration of the cases with a history of chorea does not show any striking differences from the findings for rheumatism in general, apart from a high sex incidence in females, most marked before the age of 25. There does not appear to be any association with any specific valve lesion. When all the chronic lesions are taken together, there was a history of chorea and of other acute rheumatism in 1 and 26 per cent. respectively of the males, and in 5 and 35 per cent. of the females. These figures are rather lower than those of Dunn and Hedley (1938), but they do not give details about the age and sex.

It will be seen that every attempt at correlation of chronic valve lesions with acute or recurrent endocarditis breaks down in some fundamental aspect, and that no satisfactory explanation can be offered for the sex and age differences in the various valve lesions. Nevertheless these differences appear to be important and to be of some definite significance.

SUMMARY

A statistical analysis was made of the pathological and clinical findings in 1057 necropsies on patients with acute or chronic valvular lesions, to ascertain the sex and age differences.

Chronic Rheumatic Valve Lesions.—There was a very high incidence of pure mitral lesions in young girls and of combined lesions affecting the tricuspid in women from 15 to 35. In males, combined aortic-mitral lesions were common throughout life, but tricuspid involvement was rare. The age of death in chronic mitral lesions was about the same as in chronic aortic-mitral lesions, but patients with chronic tricuspid lesions tended to die much earlier, nearly always as a result of congestive failure.

Recurrent Endocarditis.—Simple acute vegetations, developing on an old valve lesion or, less often, spreading to previously undamaged valves, were very common in childhood but progressively less frequent with advancing age. This recurrent endocarditis was rather more frequent in females; it was very common in acute rheumatism or congestive failure, but was sometimes found with intercurrent diseases. The mitral and aortic were involved with about equal frequency, the tricuspid less commonly.

Simple Acute Endocarditis.—This was rare under 5 years of age. It was more common in older children, associated with acute rheumatism or chorea or

sometimes with acute infections or septic conditions. In adults the endocarditis was usually associated with infections or miscellaneous conditions ; in old age it was usually a terminal occurrence in carcinoma or cardiorenal disease. In acute rheumatism the lesion usually affected multiple valves : in non-rheumatic cases it usually affected the mitral alone, particularly in females, or the aortic alone, particularly in males ; combined lesions were uncommon.

Ulcerative and Subacute Endocarditis.—This was rather commoner in males than in females. When occurring on previously normal valves it was usually of septicæmic type in early life ; but in old age it was often only terminal, usually in association with carcinoma of the stomach or uræmia.

When developing on previously scarred valves it was commoner in middle life, particularly in males, and was usually of septicæmic type ; it was common on chronic aortic but rare on tricuspid lesions.

Primary Sclerosis and Syphilis.—This affected the aortic valve and was commoner in males than in females.

It is difficult to obtain any real correlation between the incidence of acute endocarditis, recurrent endocarditis, and the chronic valve lesions. Some of the acute lesions may lead to subsequent scarring of the valves, and some of the recurrent lesions to increase of the fibrosis in scarred valves or to the scarring of previously normal valves. The evidence on this matter is, however, inconclusive.

We wish to express our thanks to Professor Shaw Dunn, Professor Blacklock, and Dr. Montgomery for permission to study these autopsy reports.

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STENOSIS AT THE LOWER BULBAR ORIFICE OF THE INFUNDIBULUM

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Stenosis at the lower bulbar orifice is not very rare, as Keith (1909) in the examination of two hundred and seventy abnormal hearts found it to be present in nineteen. We consider, however, that the associated abnormalities of this heart make the case worthy of publication.

The right ventricle is a composite chamber, formed partly by the transverse part of the primary ventricular loop and partly by the lower part of the bulbus cordis; the bulbus lies between the common ventricle and the truncus arteriosus in the embryonic heart. The bulbus cordis persists in elasmobranchs and most of the reptiles as a chamber that remains separate from the ventricle, but in the mammalian heart part of the bulbus is incorporated in the right ventricle. Greil (1903) was the first to suggest that the part of the bulbus absorbed by the right ventricle is represented by the infundibulum (conus arteriosus) in the adult human heart. Keith (1924) considers that the function of the infundibulum in the mammalian heart is essentially akin to that of the bulbus cordis in the lower vertebrates, in which it persists as such; that the bulbus acts as a guarding mechanism for the vascular network of the lungs against the raised blood pressure that occurs during increased cardiac activity; and that the musculature of the infundibulum passes into action later than that of the body of the right ventricle.

The component parts of the right ventricle in the human heart, however, may retain their individuality and only communicate with each other by a constricted orifice. This condition has been referred to by Keith as *stenosis at the lower bulbar orifice of the infundibulum*.

In such a heart the infundibulum itself is expanded above the orifice and forms a dilated, but relatively thin-walled chamber, which communicates freely with the pulmonary artery. The wall of the right ventricle below the orifice, i.e. the ventricle proper, is hypertrophied and is usually thicker than the wall of the left ventricle. The size of the lower bulbar orifice varies greatly in different specimens, and the duration of life tends to bear a direct relationship to the size of this orifice.

In the great majority of examples so far described there has been a deficiency

in the interventricular septum and in most of these the communication has been such as to provide a shunt between the two chambers. In four cases, recorded by Lafitte (1892), Jackson (1893), and Eakin and Abbott (1933), there was no interventricular foramen. Associated with this deficiency there is usually some degree of dextro-position of the aorta. This combination of defects is not surprising, as the incorporation of the bulbus cordis in the right ventricle normally takes place early in development before the completion of the septa and before the normal torsion of the arterial trunks. For the same reason a patent foramen ovale and a patent ductus arteriosus are sometimes found in association with these other changes.

CASE RECORD

A. L., aged 38, was admitted to the Eastern General Hospital, Edinburgh.

History.—He had "heart trouble" of unknown nature when 17 years of age, from which he recovered well. He never had rheumatic fever, but suffered frequently from sore throats, the last being one week prior to the onset of his terminal illness. Throughout his life he had been unable to take violent exercise because it caused attacks of extreme breathlessness and cyanosis. No other illnesses were admitted.

One month before admission he began to notice weakness and marked tiredness on exertion and inability to walk more than a quarter of a mile without a rest. His feet, face, and tongue began to swell. He developed a cough with sputum, and for three weeks had suffered from diarrhoea. As the condition was progressing rapidly, he was sent to hospital.

Examination.—He was of medium size, with a sallow complexion, cyanosed lips and hands, and puffiness of the face. The fingers and toes exhibited clubbing. No purpuric spots were noted. There was œdema of the feet and legs and also a small lumbar pad.

The pulse was rapid (100 per minute), regular, and of good volume. Blood pressure, 150/100 mm. The vessel walls were not palpable. The apex beat was visible and diffuse; on palpation it was forcible and was localized in the sixth interspace in the anterior axillary line. There was an apical diastolic thrill. On auscultation there was a harsh loud diastolic murmur of maximum intensity in the fourth interspace at the left border of the sternum, propagated in all directions. There was also a systolic murmur in the pulmonary area, propagated upwards for one inch towards the left.

Both bases were dull to percussion posteriorly and the respiratory sounds were diminished. The respiratory rate was 30. The sputum was slight in amount and consisted of a frothy mucus.

The abdomen was distended. The liver was not enlarged. Otherwise no abnormality was detected on clinical examination.

The urine contained much albumen and a faint trace of blood. Microscopically there were granular and epithelial casts and red blood cells. The hæmoglobin was 45 per cent.

Course.—The temperature swung between 97° and 101° during the first six days in hospital, but thereafter remained normal or subnormal. A blood culture was carried out twice during this pyrexial stage, but no growth was obtained. The œdema became worse, despite therapy. The spleen, which had not been palpable, enlarged progressively and became tender. At no time were any purpuric spots noted. The patient remained lethargic in his reactions for the first week, after which he became more torpid and eventually died in a coma two weeks after his admission.

Summary of Autopsy Findings.—The body was moderately developed. There was slight but generalized œdema. The pericardial and peritoneal sacs contained several

ounces of clear serous fluid. Both pleural cavities were almost obliterated by dense fibrous adhesions.

The heart exhibited gross abnormalities which are given in detail below. The outstanding feature was the tremendous hypertrophy of the right ventricle.

Both lungs were congested and slightly œdematous towards their bases ; no infarcts were detected.

The spleen weighed 750 g. No infarcts were present in the spleen or in the kidneys, both of which showed gross congestion.

No congenital abnormality was detected apart from that noted in the heart.

ANATOMICAL FEATURES OF THE HEART

The chief abnormalities present were : (a) stenosis of the infundibulum (conus arteriosus) at the lower bulbar orifice ; (b) hypertrophy of the right ventricle below the orifice ; (c) dilatation of the infundibulum ; (d) communication of the right ventricle with the anterior sinus of the aorta ; and (e) a small communication between the right and left ventricles.

The heart showed general enlargement (550 g. compared with an average of 330 g.), especially of the right auricle, which was markedly dilated, and of the right ventricle, which was more conspicuous than usual in the region of the infundibulum.

The walls of both right chambers were thickened. The wall of the right auricle had an average thickness of 4 mm., with prominent muscoli pectinati ; the wall of the left auricle was 2 mm. thick. Beneath the anterior limb of the limbus of the fossa ovalis there was an oblique passage 10 mm. long just admitting a fine probe. This is the standard type of patent foramen ovale which is found in a large percentage of hearts (25–30 per cent.).

The right ventricle was subdivided by an obliquely placed septum into (a) the right ventricle proper and (b) the infundibulum (conus arteriosus) ; the only communication between these two subdivisions was a foramen in the septum which measured 7 × 5 mm. ; the edges of the foramen were white and fibrous. The general disposition of these parts of the chamber are shown in Fig. 1.

The wall of the ventricle proper was especially noteworthy on account of its unusual thickness. Near the lower margin of the heart it was 13 mm. thick, gradually increasing towards the base of the chamber to 24 mm. ; the thickness of the ventricular septum was, on an average, 15 mm., with a corresponding increase in the trabeculæ carneæ, moderator band, and papillary muscles. The tricuspid orifice in the fresh specimen was large enough to admit five fingers ; the chordæ tendineæ were much thicker than usual and near the cusp margins flattened out into membranous bands.

About 10 mm. in front of the left end of the base of the anterior cusp there was an opening, with a maximum diameter of 7 mm., that led into the aorta. The margins of this orifice were thin and membranous and in the fixed specimen had come together so as to occlude the passage. This connection between the right ventricle and the aorta indicates that there was some dextro-position of that vessel. The site of the upper opening of the orifice was especially note-

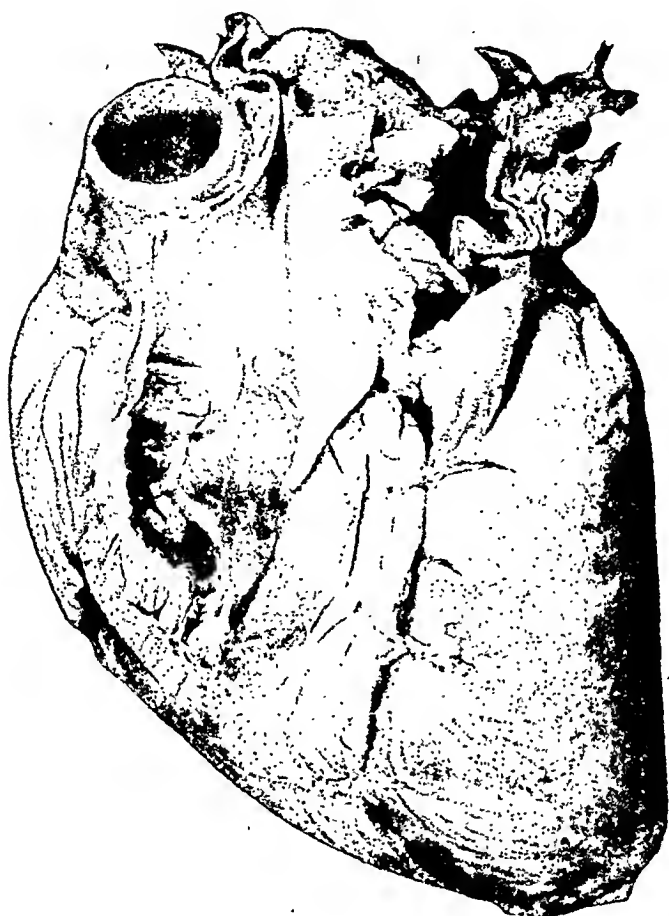


FIG. 1.—Anterior view of the heart. The interior of the infundibulum and the communication of this chamber with the body of the right ventricle is shown.

worthy in that it was actually into the anterior sinus—which was much enlarged—and was about 10 mm. below the origin of the right coronary artery.

Immediately behind the aortic opening, i.e. between it and the tricuspid valve, there was a small, slit-like orifice, 3 mm. long and just large enough to admit a fine probe, leading into the aortic vestibule. The opening of this communication into the right ventricle was so guarded by a flap-like fold of endocardium that, quite apart from its size, there could be little doubt that it had not functioned during life.

The infundibular part of the right ventricle (Fig. 2) was much enlarged. In general it had a slightly saccular form, with a maximum length of 31 mm. and a width of about 20 mm. The posterior wall of the chamber was smooth, but the anterior wall was roughened by several well-defined trabeculæ carneæ.



FIG. 2.—Anterior aspect of the heart. The interior of both the right and the left ventricles is shown and three arrows have been inserted to demonstrate the communications between the chambers. The *black* arrow has been passed from the body of the right ventricle into the infundibulum; the *stippled* arrow passes from the left ventricle into the aorta; and the *white* arrow from the right ventricle into the aorta.

The opening into the right ventricle proper was on the right wall of the chamber about 13 mm. above its most dependent part; above, the chamber communicated freely with the pulmonary artery through the pulmonary valve. The cusps of the pulmonary valve had the normal anatomical arrangement and showed no stenosis. The wall of the chamber was not of equal thickness throughout, as in its lowest part it varied from 5 to 9 mm. and as it was traced upwards it gradually thinned and so imperceptibly merged with the wall of the pulmonary artery.

The wall of the left ventricle was relatively thin as compared with the right, as near the base of the heart it was 14 mm. (cf. 24 mm. in the right) and at the apex it was 7 mm. (cf. 13 mm. in the right). The aortic orifice was displaced slightly to the right.

The diameter of the aorta was 21 mm. as compared with 17 mm. in the pulmonary artery; in the normal heart the pulmonary artery is slightly wider at its origin than the aorta.

Pathological Features.—In addition to these anatomical abnormalities there was endocarditis involving the opening between the right ventricle proper and the infundibular portion. Large fungating vegetations completely surrounded the orifice. No ulceration of the wall in this area could be detected, but the vegetations extended upwards from the orifice on to the wall of the conus arteriosus and involved the cusps of the pulmonary valve. They were growing through the orifice also and protruding into the right ventricle.

Microscopically.—The vegetations consisted of a fibrin thrombus with organization in its base; this and the adjacent muscle was densely infiltrated with cells in which polymorphs were prominent. On the surface of the vegetations were clumps of cocci. On the conus side of the pulmonary valve there was a similar formation, but with a more cellular fibrosis and less cellular infiltration and fibrin clot. A large patch of hyalinized fibrous tissue in the wall of the conus had apparently arisen from the overlying endocarditic changes. The myocardial fibres underlying the endocarditis were somewhat hyalinized, and in the right ventricle showed considerable hypertrophy. There was some periarterial fibrous thickening, and thin strands of connective tissue could be seen extending out between the muscle bundles from the vessels. This feature was much more marked in the right ventricle than in the left. No Aschoff nodules were present, but there was some intimal thickening with scarring in a few of the smaller myocardial vessels. This was obviously of long standing, but was not specific enough to warrant a diagnosis of an old rheumatic lesion. The wall of the right auricle contained more fibrous and less elastic tissue than did that of the left. As compared with a normal heart, however, this variation was not so prominent as was the relative difference in the ventricles with the definite fibrosis in the wall of the right chamber.

DISCUSSION

The case is a typical example of stenosis of the lower bulbar orifice of the infundibulum. Associated with this stenosis there was hypertrophy of the wall of the right ventricle, a minute opening in the ventricular septum, and a slight degree of dextro-position of the aorta.

The stenosis of the lower bulbar orifice in this case was essentially similar to that found in the cases of this anomaly reported previously. In these the measurements showed a wide variation, but the size in this specimen (7×5 mm.) was less than usual. The position of the orifice was not as usually described, however, as it was not in the most dependent part of the infundibulum, but about 13 mm. higher. The stenosed orifice was quite unguarded by any valvular mechanism and was probably responsible for the murmurs heard during life, though the vegetations around the orifice might have exaggerated them. The presence of bacterial endocarditis at the site of

the anomaly is in keeping with the view that such a lesion tends to occur in association with some pre-existing malformation.

The hypertrophy of the wall of the right ventricle proper was undoubtedly due to the small size of the pulmonary outlet. Associated with this hypertrophy there was a patchy fibrosis throughout the wall of this ventricle which was absent from the left ventricle. This fibrosis was, if anything, more pronounced in the subendocardial region of the myocardium, as had already been observed in a similar case reported by Eakin and Abbott (1933).

The opening in the ventricular septum was small and as it was guarded on the right side by a flap-like fold of endocardium it is felt there could not have been a veno-arterial shunt. Hence this case may be classed with these where the septum is complete. As already stated, stenosis of the lower bulbar orifice is generally found with a large defect in the ventricular septum, which allows free communication between the pulmonic and systemic circulations, so that these patients always have a slight cyanosis. The present case, however, only showed cyanosis during exertion, and it is justifiable to infer, therefore, that this must have been due to the stenosed bulbar orifice rather than to a veno-arterial shunt. This stenosis, while allowing a sufficient passage for normal activities, would interfere with the additional flow of blood that would usually pass to the lungs on exertion.

The aorta showed some degree of dextro-position and the manner of connection between the right ventricle and this vessel was of special interest. The opening was between the highest part of the right ventricle and the enlarged anterior aortic sinus, about 10 mm. below the origin of the right coronary artery. The orifice, which was 7 mm. in diameter, had a fibrous ring projecting into the sinus in the form of a cone. Probably, therefore, this had a valvular action and prevented the regurgitation of aortic blood in the right ventricle during diastole. This mode of communication, whereby the right ventricle opens into the aortic sinus, has never been recorded before so far as we are aware. The proximity of this ventriculo-aortic communication and the origin of the right coronary artery suggests that the former might have been responsible, by interfering with the blood supply, for the undue fibrosis present in the wall of the right ventricle.

SUMMARY

A heart is described in which there was stenosis of the lower bulbar orifice of the infundibulum. This feature is not in itself rare, but the absence of a functional interventricular foramen makes the case unusual. The communication of the right ventricle with the anterior aortic sinus is a further feature of interest.

Despite the gross abnormalities that were present in the heart, the subject lived to the age of thirty-eight, when the occurrence of bacterial endocarditis was responsible for death.

We are indebted to Dr. R. B. McMillan, Superintendent of the Eastern General Hospital, Edinburgh, for permission to publish the clinical notes of this case. We should also like to express our thanks to Professors W. T. Ritchie and A. M. Drennan for their interest and helpful criticism.

The photographs were taken by Mr. T. C. Dodds of the Pathology Department, Edinburgh University.

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VOLUMETRIC RECONSTRUCTION OF THE HEART IN HEALTH AND IN DISEASE: A RADIOLOGICAL STUDY

BY

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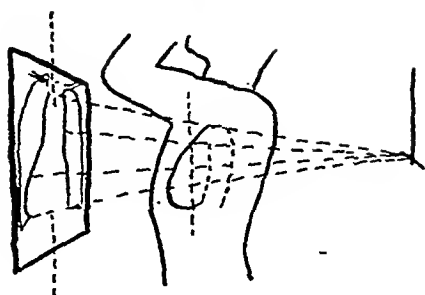
Radiological study of the heart has now become a well-recognized and valuable procedure in the investigation of a cardiac patient; certain changes in heart shape and size can only be demonstrated by this method. The rationale of fluoroscopy of the heart is that by rotating the patient into suitable positions each chamber may be made to form a border, so that a measure of its size and depth is obtained. The value and limitations of the radiological approach can be estimated only on the basis of a knowledge of the relative size and position of these chambers. To the student fresh from the dissecting and post-mortem rooms there is a bewildering difference between the configuration and relative anatomy of the heart chambers before and after removal of the organ from the body. To help to obviate this difficulty it was thought worth while to reconstruct, in permanent form, a series of life-size models of normal and diseased hearts, the study of which would enable the student to appreciate more readily the radiological changes of heart disease. This paper deals with the manner of their reconstruction, with a description of each model. In addition, a few remarks about some more or less controversial points in the gross anatomy of the heart and great vessels are included.

THE METHOD OF RECONSTRUCTION

The first step in the procedure was devised by Palmieri (1921) and, although in itself it has not any important clinical application, it provides us with a clay replica of the heart that forms the basis of our final reconstruction; in Fig. 1 is illustrated the principle of the method.

First Stage.—This is entirely a fluoroscopic procedure, the object being to obtain a series of tracings of the cardiovascular silhouette in different degrees of rotation of the patient. The patient is placed on a revolving stool, the vertical axis of which passes approximately through the centre of the heart. The X-ray tube is at the ordinary distance from the patient. The distances of the tube from the heart axis and from the fluoroscopic screen are measured and recorded; these are kept constant in all examinations. By central (not

1st STAGE



2nd STAGE

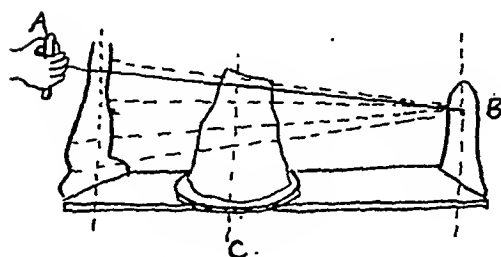


FIG. 1.—Diagram illustrating Palmieri's method of radiological volumetric reconstruction of the heart. *First stage*: by fluoroscopic examination in different degrees of rotation of the patient tracings are obtained of the cardiovascular silhouette by central projection. *Second stage*: the tracings are cut out in cardboard and, with the apparatus shown, a length of wire AB is moved along the edge of the cardboard section and pieces from a block of plastic material C are cut off. With each cardboard section the block is rotated into the corresponding position. When the manoeuvre is completed a replica of the heart is obtained. (Modified from Palmieri (1921).)



FIG. 2.—Clay replica of a normal heart obtained by Palmieri's method. Anterior, left and right oblique views.

orthodiagraphic) projection a tracing of the heart and great vessels is made on the screen in the anterior position. The tracing is made with lipstick so that a sheet of paper pressed against the screen will record the outline obtained.



L.O.

ANT.

R.O.

FIG. 3.—Clay replica of a normal vertical heart, with low diaphragm. Anterior, left and right oblique views.

The markings on the screen are then erased, the patient rotated through 30 degrees and a second tracing made. Of course, the heart shadow must be centred before each tracing. The use of lipstick renders it possible rapidly



L.O.

R. O.

ANT.

FIG. 4.—Clay replica of a normal transverse heart, with high diaphragm. Anterior, left and right oblique views.

to transfer the tracing from screen to paper in the dark, thus avoiding the necessity of interrupting the pupillary accommodation. Twelve tracings are made of the heart outline in different projections by rotating the patient through 360 degrees. The angle at which each drawing is made is recorded. Certain



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FIG. 5.—Clay replica of heart in case of mitral stenosis. Prominence of left pulmonary artery and conus in anterior view; bulging of left auricle in right and left oblique views; enlargement of right side of heart. Anterior, left and right oblique views.

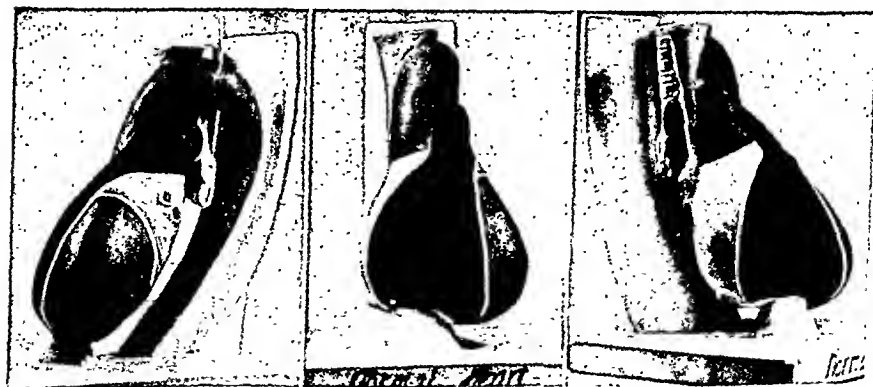


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FIG. 6.—Clay replica of heart in case of free aortic regurgitation, showing prominent aortic knob and enlargement of left ventricle. Anterior, left and right oblique views.



ANT.

R.O.

FIG. 7.—Model 1. Average normal heart. A modification of Taipale's model (1934). The correct juxtaposition of œsophagus and arch of the aorta is shown; the convexity of the right heart border has been reduced by narrowing the width of the base of the right ventricle; the apex of the heart is formed entirely by the left ventricle; the left auricular salient is reduced.

difficulties arise which make it impossible to obtain a *complete* outline in every view. The diaphragmatic surface of the right ventricle is not visualized in the anterior view ; in young people the arch of the aorta and the posterior border of the left auricle are difficult to make out in the left lateral and oblique views ; in the postero-anterior view, the upper segment of the left heart border is partly hidden. In spite of these limitations, prolonged accommodation of the eyes in the dark room and repeated examinations made it possible to obtain such tracings in a number of patients with the commoner forms of heart disease.

Second Stage.—The paper tracings are cut out in stiff cardboard and, with the apparatus shown in Fig. 1, a replica of the heart is cut off from a block of plastic material. The apparatus consists of a plank of wood equal in length to the measured distance between the X-ray tube and the screen. At C, a point corresponding to the vertical axis of the revolving stool (and of the

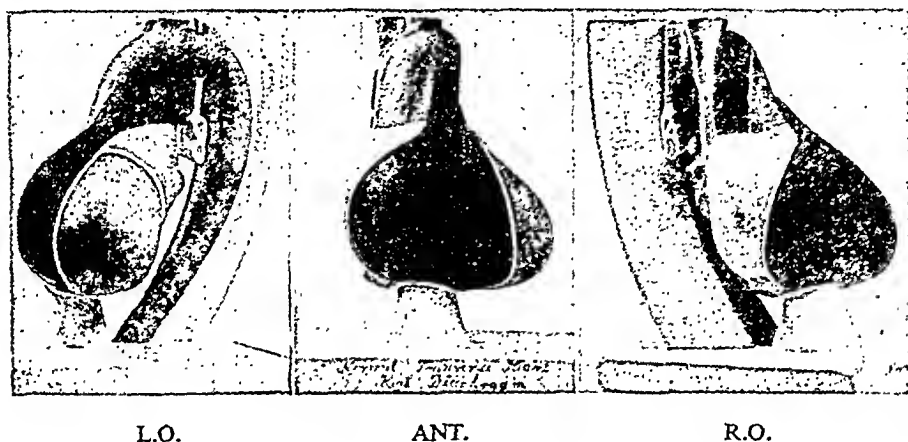


FIG. 8.—*Model 2. Transverse type of heart.* The axis is approximately at right-angles to the great vessels. The level of the cardio-aortic junction is raised and the vascular pedicle is shortened. The transverse diameters of heart and vascular pedicle are increased. In the left oblique view the arch of the aorta is curved on a large radius. The retrocardiac space is increased.

patient's heart), a hole is bored and over this is placed a disc of wood marked off in degrees. A block of soft artist's modelling clay is centred about this axis on the wooden disc. At one end is a wooden upright to which is fastened a length of piano wire AB ; the point B corresponds to the position of the centre of the X-ray tube. At the other end are placed two grooved uprights which serve to hold the cardboard sections in position. Thus the screen is replaced by the cardboard sections, the body of the patient by a block of plastic material, and the tangential X-ray beam by the length of piano wire.

The first cardboard section, showing the cardiovascular silhouette in the anterior view, is placed in position and the wire moved along the edge ; and in so doing it cuts off a part of the clay. The latter is then rotated through 30 degrees when the corresponding section is inserted and the manœuvre repeated. When each heart outline has been cut and the clay has been rotated through 360 degrees, the replica of the heart is complete. It is a fairly accurate

reconstruction of the body of the heart and part of the aortic arch. Such clay models then serve as the foundation for our final reconstruction. Figs. 2, 3, 4, 5, and 6 illustrate plaster casts of such clay replicas.

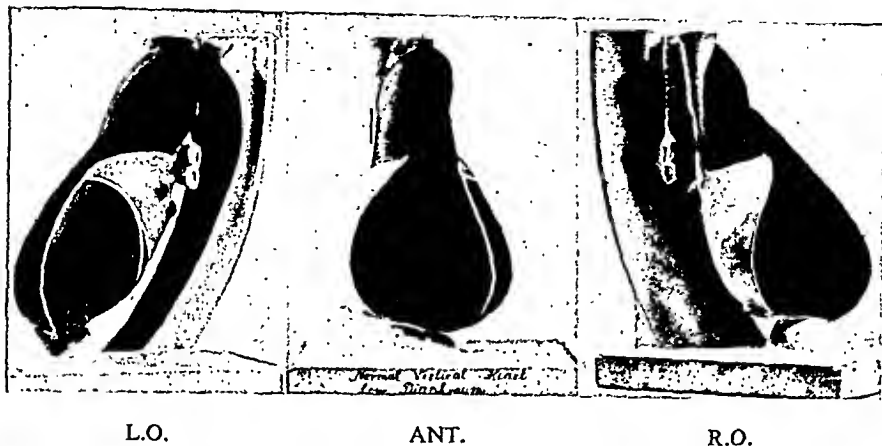


FIG. 9.—*Model 3. Vertical type of heart.* The transverse diameters of the heart and the vascular pedicle are both reduced. The diaphragm is low in position and the convexity of all contours in all views is only slightly prominent. The right ventricle may participate to a small degree in the right heart border. The arch of the aorta appears short in the left anterior oblique view and is curved on a small radius. Both the dorsal and ventral cardiac contours are rather flat. The retrocardiac space is comparatively small.

Third Stage.—Palmieri's reconstruction did not proceed beyond the second stage. However, Taipale (1934) has constructed a porcelain model of a normal

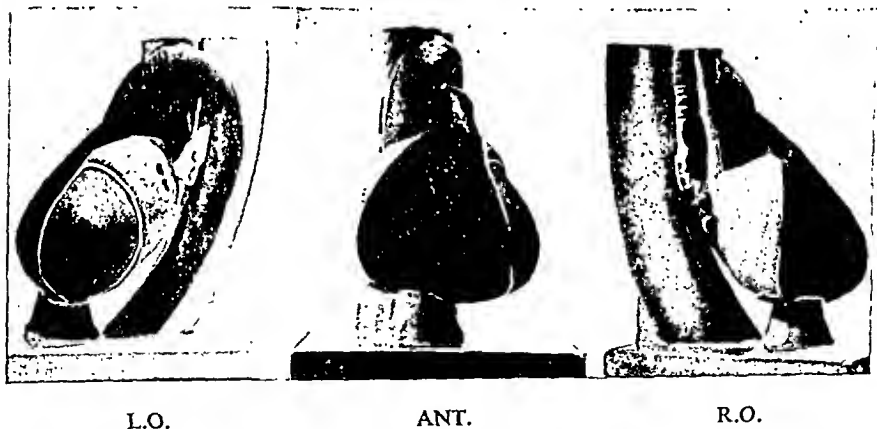


FIG. 10.—*Model 4. Moderate mitral stenosis.* Anterior view shows straightening of left heart border, due to prominence of pulmonary artery and conus and left auricle. Moderate dilatation of the pulmonary artery. Left anterior oblique view shows enlargement of the left auricle. The retrocardiac space is diminished especially in its upper and middle thirds. There is no elevation of the left main bronchus.

heart which was based on many fluoroscopic examinations. Although not free from error, it is undoubtedly one of the most useful models yet made, especially from the radiological point of view. For this reason, and because

of the high degree of artistic finish of the model, it was decided to fashion our own abnormal models on similar lines, but owing to the prohibitive cost of porcelain manufacture it was arranged to cast our model in plaster.

A wooden armature was constructed, consisting of a base, $7\frac{1}{2}$ inches square and 1 inch in thickness, with an upright $8\frac{1}{2}$ inches in height carved to represent the vertebral column. The clay replica was placed in position in front of the column, supported on a wooden pedestal and transfixed in its vertical axis by a screw driven through the base. With this as a foundation, the position of the heart chambers, interventricular, and auriculo-ventricular grooves were indicated and the great vessels, œsophagus, and trachea built up according to their position as outlined at fluoroscopy. Deviations of the œsophagus were

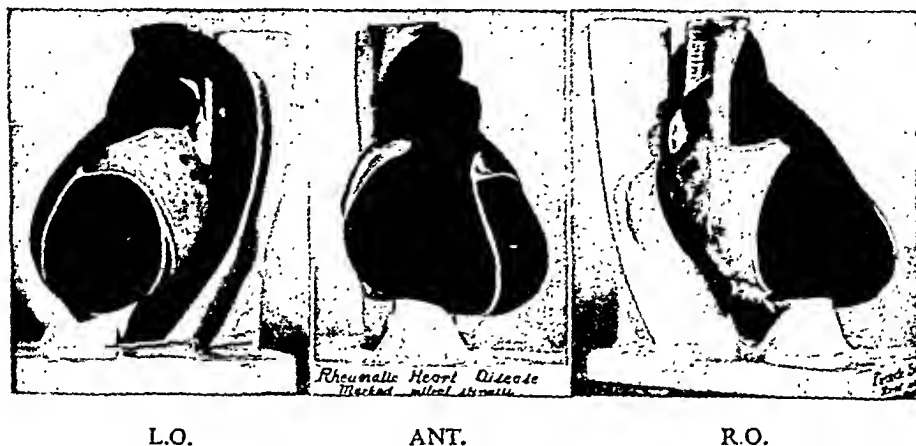


FIG. 11.—Model 5. *Marked mitral stenosis.* Left auricular enlargement causes a convexity on the left heart border below the dilated pulmonary artery and conus. In the anterior view the left auricle can be seen on the *right* border of the heart, projecting above and behind the right auricle. Enlargement of the left auricle has obliterated the upper two-thirds of the retrocardiac space and has elevated the angle of bifurcation of the trachea and left bronchus. The œsophagus is displaced to the right by the enlarged left auricle and takes a wide sweep before it crosses to the left side of the descending aorta just above the diaphragm. In the lateral view the prominent pulmonary artery and conus make the anterior heart border convex. There is moderate dilatation of the right ventricle and right auricle.

detected by a barium swallow, and the position of the trachea recorded as accurately as possible. It was not considered necessary to outline the tracheal bifurcation with lipiodol. The intraventricular notch could not be visualized in each case and the position of the auriculo-ventricular grooves had to be obtained from observations on post-mortem controls. The position of the diaphragm was indicated by raising or lowering the pedestal upon which the heart rested. Except when the width of the descending aorta could be readily measured, an average was struck and maintained in all models in which the aorta was normal.

On completing such a model in clay, it was cast in plaster, shellacked, coloured, and inscribed. Twelve such models have been completed and they are illustrated in Figs. 7–18 of this paper with a description of each, with photographs in the anterior, left oblique, and right oblique views.

SOME ANATOMICAL COMMENTS OF RADIOLOGICAL INTEREST

One error in Taipale's model of the normal heart needed correction ; it concerned the position of the œsophagus in its relationship to the arch of the aorta. Taipale failed to show that the œsophagus normally receives an

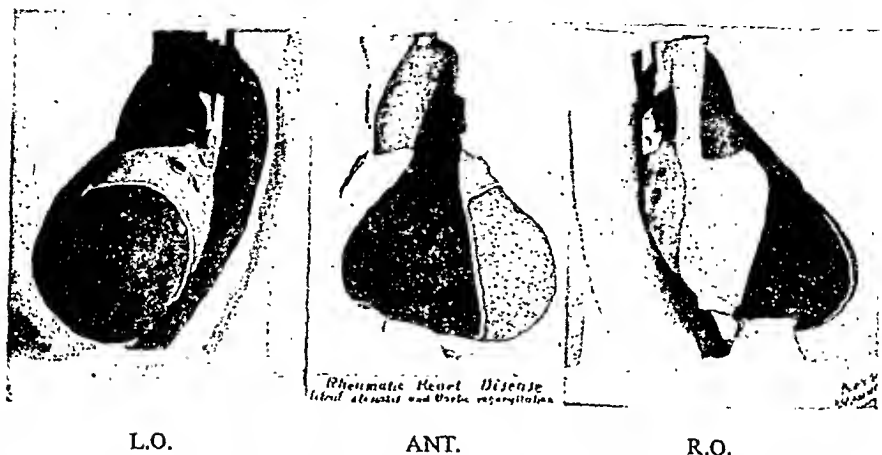


FIG. 12.—*Model 6. Mitral stenosis and aortic regurgitation.* Besides the features of mitral stenosis, as described in Model 5, there is also marked left ventricular enlargement, due to aortic incompetence. In the left oblique view the lower third of the retrocardiac space is largely obliterated by the enlarged left ventricle.

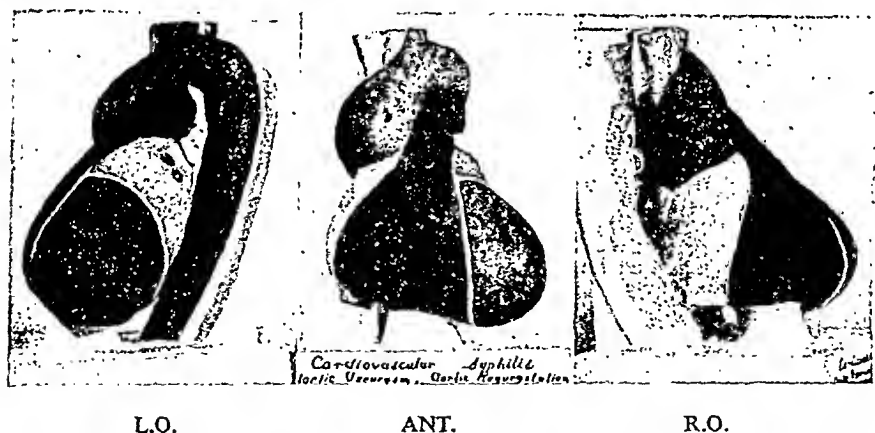


FIG. 13.—*Model 7. Aneurysm of the ascending limb of the aortic arch, with aortic incompetence.* The left ventricle is enlarged. The aneurysm projects to the right beyond the right margin of the superior vena cava, which is displaced posteriorly and to the right. The aortic knob is prominent, presenting a marked convexity on the upper left border of the vascular pedicle. The trachea and œsophagus are displaced posteriorly and the latter is compressed against the vertebral column.

impression, roughly 3 cm. in length, from the right wall of the aortic arch just as that vessel begins to descend (Evans, 1936). In his model there is a distinct gap at this level due to the displacement of the œsophagus to the right.

Somewhat more debatable but no less important features are the degree of prominence of the right heart border and the width of the base of the right

ventricle. In the anterior view the right border, correctly shown to be entirely composed of the right auricle, is too prominent, while the width of the base of the right ventricle is exaggerated. The latter measurement places the interventricular groove and notch rather to the left of the normal, so that the heart apex comes to be formed by both right and left ventricles. This is undoubtedly not true in the normal heart, in which the apex is formed solely of left ventricle. For these reasons we have modified Taipale's model and constructed what we regard as an average normal heart (Fig. 7, Model 1).

The Superior Vena Cava.—Studies of the normal heart post-mortem, after radio-opaque injection, and observations upon the wax-injected heart in situ indicate that the true position of the superior vena cava in relation to the ascending limb of the aortic arch is not properly appreciated. Illustrations of the heart in most anatomical texts and the majority of papier-mâché composition

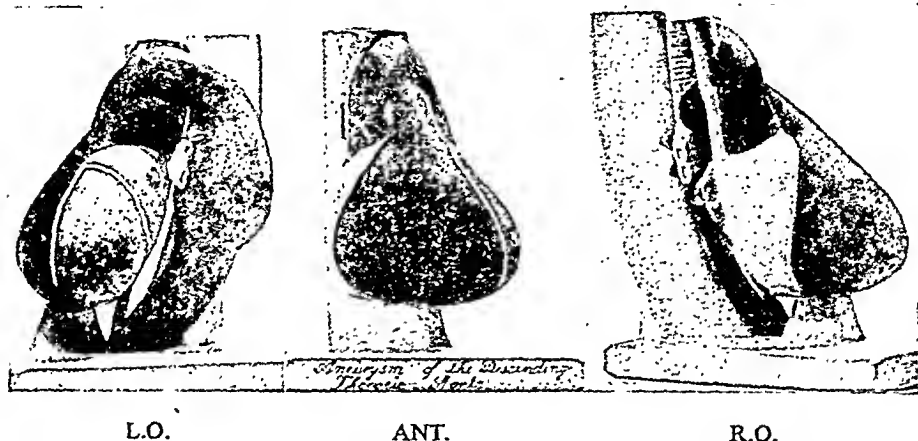


FIG. 14.—Model 8. *Aneurysm of the descending thoracic aorta.* The heart size and configuration are normal. In the anterior view, the dilated descending aorta is seen well to the left, disappearing behind the heart at the level of the junction of the left auricle and left ventricle. In the left oblique view, the aneurysm, fusiform in type, is seen projecting beyond the left margin of the vertebral column, eroding the latter and adherent anteriorly to the left bronchus, which is stenosed and deformed. In the right oblique view erosion of the anterior aspect of two adjacent vertebrae is seen.

models in anatomical museums portray the superior vena cava as lying well to the right and only slightly posterior to the root of the aorta. This is quite inaccurate. The superior vena cava lies almost wholly posterior to the root of the aorta and rarely projects more than half a centimetre beyond the right aortic border at this level. Thus in a telerradiogram or orthodiagram the right border of the vascular pedicle in its lower third indicates the position of the right border of the ascending aorta. Mainly concerned with the dried, preserved corpse, the anatomist has for decades depicted these two vessels lying in practically the same plane.

The Right Ventricle.—The right border formed by the right ventricle has likewise been inaccurately depicted. If a glass plate is placed over the opened thorax of the corpse and a tracing is made of the heart outline, it will readily be seen that, when it is compared with an orthodiagraphic tracing of the

same patient taken during life, the right heart border is formed entirely by the right auricle. In the anterior view the right ventricle takes no part in the formation of the lateral heart borders. One exception might be mentioned, namely, the "drop" heart found in tall, spare individuals with a low diaphragm,

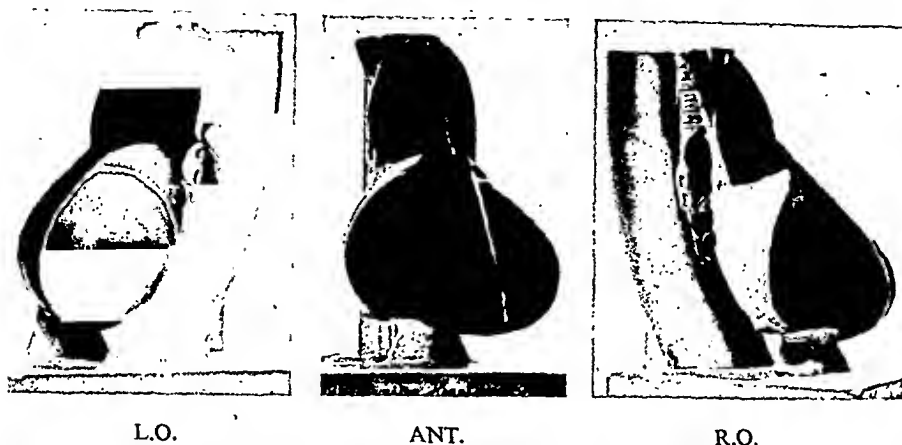


FIG. 15.—*Model 9. Hypertensive heart and tortuous arteriosclerotic aorta.* Characteristic enlargement of the left ventricle and also widening and tortuosity of the whole aorta. In the anterior view, the ascending limb projects to right of the superior vena cava, while the arch runs obliquely backwards to the left, instead of almost directly backwards. The aortic knob is accentuated and the whole arch takes a wide curve, due to lengthening of the aorta. The descending aorta projects posteriorly and to the left and its lower third is kinked as it passes forward to descend through the diaphragm.

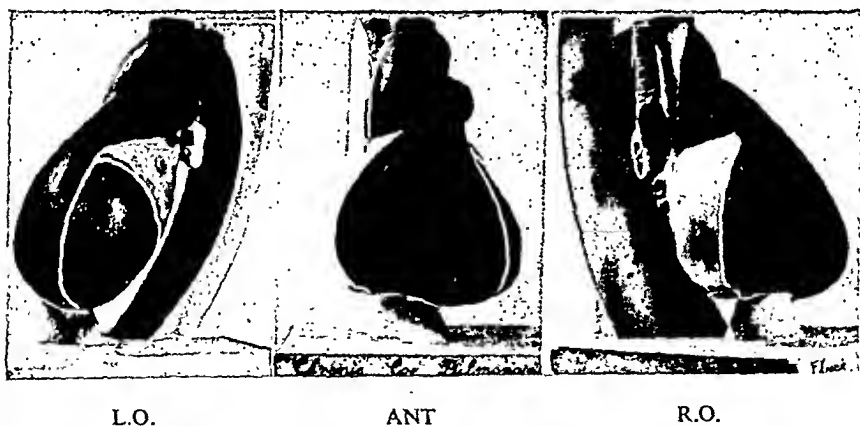


FIG. 16.—*Model 10. Chronic cor pulmonale.* Enlargement of the right ventricle and pulmonary arterial trunk. In the anterior view the pulmonary artery and conus are prominent and form a marked convexity on the left heart border. In the lateral view the anterior border of the heart presents a marked prominence in the region of the conus due to enlargement of the outflow tract of the right ventricle.

in whom the right ventricle may take part in forming a very small segment of the right heart border near the entrance of the inferior vena cava. This point is of some importance as it means that slight enlargement of the right ventricle is not detected in the anterior view; the outflow tract, which is the first to show signs of enlargement, can only be viewed in the oblique or lateral positions.

The Left Auricle.—Whether the left auricle takes any part in the formation of the left heart border has been the subject of much debate ; modern opinion is that it does not. Indisputable evidence on this point is difficult to obtain, but the impression one has obtained during the course of this study is that,

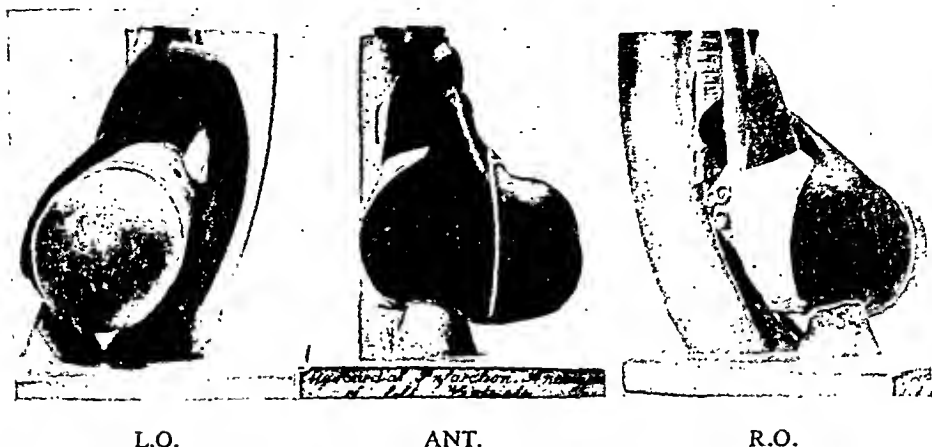


FIG. 17.—*Model 11. Myocardial infarction and aneurysm of the left ventricle.* Boot-shaped appearance of the heart in the anterior view, due to bulging of the left ventricle near the apex. The ventricle projects to the left and posteriorly, is rounded in shape and presents a shallow concavity on its left lateral margin. In the right oblique view there is characteristic "ledging" as the aneurysmal sac bulges forward from the main cardiac mass. In the left oblique view the retrocardiac space is reduced in its lower third.

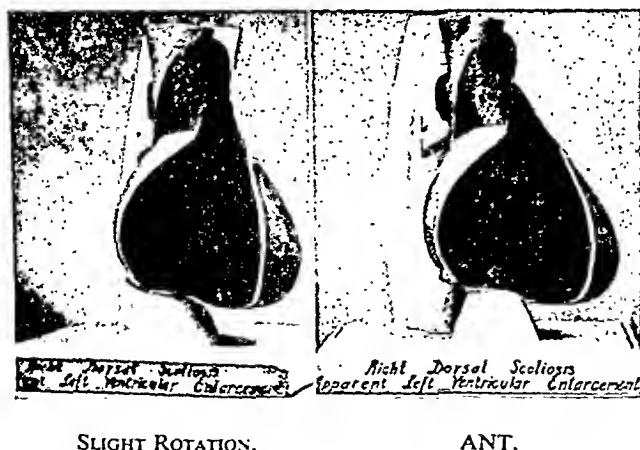


FIG. 18.—*Model 12. Right dorsal scoliosis with apparent left-sided enlargement of the heart.* The moderate, adolescent type of scoliosis gives the impression of left-sided cardiac enlargement with prominence of the aortic knob. When rotated slightly to the right, however, the scoliotic effect is counterbalanced and the heart appears normal. (Parkinson, 1936.)

certainly in some cases, a small segment between the pulmonary artery and left ventricle is formed by the triangular auricular appendage and adjacent wall of the left auricle. In our modification of Taipale's model of a normal heart we have reduced the auricular salient from 3 cm. to 1.5 cm. A longer arc

is only likely to occur in the "vertical" heart with a long, almost perpendicular, pulmonary artery.

The Pulmonary Arc.—Reference should be made, in passing, to the misconception that prevails in some quarters that the second curve on the left heart border in the telerradiogram or orthodiagram is formed by the conus of the right ventricle. It is sometimes loosely referred to as the "pulmonary conus." The conus of the right ventricle, however, lies well within the limits of the heart shadow in the anterior view. The pulmonary arc is formed by the trunk and left main branch of the pulmonary artery. An opportunity of making direct observations on this question has recently been afforded R. E. Gross (1939) during his operation for ligation of the patent ductus arteriosus. In several cases he states that he has observed the pulmonary arc to be formed mainly by the left pulmonary artery; clips placed on this vessel at operation delimited the pulmonary arc in a subsequent telerradiogram.

SUMMARY

A technique has been described whereby life-sized models of the heart in health and disease have been reconstructed. A description of each model in a series of twelve has been furnished, together with photographs of each in the anterior, left oblique, and right oblique views.

With the co-operation of the American Heart Association it has been possible to arrange for their distribution to those interested, in the hope that they will prove useful in the teaching of cardiology and of fluoroscopy of the heart. Enquiries should be addressed to the American Heart Association, Radio City, 50 West 50th Street, New York City, U.S.A.

I wish to tender my acknowledgments and thanks to Dr. Paul D. White for much helpful guidance and criticism during the course of this study, undertaken while holding a Commonwealth Fund Fellowship in the Department of Cardiology, Massachusetts General Hospital, Boston.

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THE KINKED CAROTID ARTERY THAT SIMULATES ANEURYSM

BY

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During the last fifteen years we have observed a number of patients in whom there was a pulsating vascular swelling at the right side of the root of the neck which at first sight suggested a carotid or innominate aneurysm. Subsequent investigation enabled aneurysm to be excluded and proved the vascular swelling to be a tortuosity or kinking near the origin of the right carotid. Often the pulsating tumour was the main or the sole complaint, and sometimes surgical treatment for aneurysm had been contemplated.

HISTORICAL

Coulson (1852) described a woman, aged 82, "who for some years before her death had a pulsating tumour, of the size of an orange, just above the right clavicle, in the situation of the carotid. The swelling had not of late increased in size and caused no inconvenience; the woman died from natural decay. The vessels arising from the aorta were elongated and considerably dilated; and the tumour, which was considered before death to be aneurysmal, consisted of a reduplication of the right common carotid. The interior of the vessels was highly vascular and there was considerable atheromatous deposit."

Hulke (1893) described a case like that of Coulson's, but without necropsy. She had "a conspicuous pulsating swelling which projected the sterno-mastoid muscle" and was thought to be an aneurysm of the common carotid artery. He concluded that the swelling was formed by a long loop of the carotid artery, comparable with the tortuosities found in more superficial arteries.

Douglas Powell (1909) reported upon a female, aged 78, with a pulsating tumour presenting the character of an aneurysm about the size of a walnut. It was defined as a widened, bent, and slightly twisted carotid artery. It proved to be a high division of the innominate artery, with a twisted kinked [*sic*] condition of the carotid, the walls of which were atheromatous and partially calcareous. At necropsy, "The right carotid was tortuous and considerably displaced. It was twisted to the right, forming a marked curve, about one-third of a circle; it also showed antero-posterior deviation as well. The right

subclavian was likewise tortuous and directed at first somewhat backward, so that the innominate appeared to be slightly twisted. The left carotid and subclavian were normal in course. The aorta, right carotid, and subclavian all showed marked signs of atheroma" (Fig. 1). In the same paper he also



FIG. 1.—Sir R. Douglas Powell's specimen of kinked carotid, showing high bifurcation of the innominate. (*Middlesex Hospital Journal*, 13, 2, 1909.)

referred to a woman, aged 60, whom he had seen fifteen years previously. She had a "degenerated, bent, and throbbing carotid artery which had simulated aneurysm, but it was clear on careful manipulation that the condition was a bent artery with locomotor impulse."

Stadler and Albracht (1911) attributed a similar swelling at the root of the neck to sclerosis and dilatation of the innominate artery. Hirschfelder (1918), in describing a case where a tortuous subclavian artery presenting its convexity in the supra-clavicular fossa had previously been diagnosed as aneurysm, noted the simulation of aneurysm by a tortuous carotid or subclavian artery. Balfour (1898), in a chapter on the simulation of aortic aneurysm by malposition of the aorta due to rickets, gave details of a woman, aged 46, who had severe dorsal scoliosis with convexity to the right and some kyphosis. She had noticed a throbbing swelling in her neck "as large as a hen's egg." In the lower part of the neck, just over the suprasternal notch, a pulsating tumour was felt crossing the trachea and dipping beneath the right sterno-mastoid muscle. At necropsy the heart was tilted up and the great vessels were displaced. The ascending aorta passed outwards to the right more than usual and continued into the transverse part at a somewhat acute angle. The innominate artery

was two inches long and twice its usual diameter. It came off from the aorta farther to the left than usual, coming to the surface at the left sterno-clavicular articulation and then crossing the trachea in the lower part of the neck to the edge of the right sterno-mastoid muscle, beneath which it dipped and divided.

Brown and Rowntree (1925) drew wider attention to the condition by publishing a series of five cases, all women, with pronounced pulsation of the lower right cervical region beneath the sterno-mastoid muscle. All their patients had hypertension. They attributed the condition to kinking or buckling of the right common carotid artery caused by the adjustment of a lengthened carotid artery to the decreased distance from the aorta (which is elevated) to the skull. They concluded that this kinking depends upon hypertension and does not result from arteriosclerosis alone.

Beardwood (1931) described two cases of hypertension, one a male, with this type of pulsation. He attributed the kinking to the fact that the carotid is fixed to some extent at its distal end, and that the aorta in enlarging pushes up the innominate artery almost out of the chest cavity. Additional examples, all women with hypertension, have been reported by O'Malley (1924), Eastwood (1927), Stolkind (1934), and Holst (1934). Recently Torrens and Horton (1938), in describing two more cases, state that none has yet been reported without hypertension. White (1937) refers to this pulsation, which he attributes to two factors—firstly vascular dilatation and secondly elevation of the great vessels by cardiac enlargement and a high diaphragm.

A somewhat similar condition due to elevation of the subclavian artery, especially the right, was described by Faure (1874) as a sign diagnostic of a dilated aorta. He described six cases, three with necropsies, in which there was elevation of the innominate artery with tortuosity of the subclavian. Barié (1912) also refers to this sign. The abnormal pulsation is at the root of the neck on the right side, but external to the sterno-mastoid. Norris and Landis (1933) also attribute "marked pulsation just above and to the right of the sterno-clavicular joint" to lifting up of the subclavian artery as the result of dynamic or passive dilatation of the arch of the aorta.

CLINICAL FEATURES

The typical patient is a woman, middle-aged or elderly, often stout, and affected by kyphosis and scoliosis. A pulsating swelling is seen and felt behind the sternal head of the right sterno-mastoid, often extending beyond the inner or the outer border or even both borders of that muscle. A drawing of the neck showing a common position of the swelling is shown in Fig. 2. The pulsation is expansile and forcible, and the excursion to the right may attain 1-2 cm. The swelling is either rounded or ovoid, with its long diameter more or less vertical. In favourable cases, careful palpation with the finger-tips shows that it consists of a vascular loop—a bend or kink in the course of the right carotid artery. The size of the swelling is little affected by posture, though it may be a little more noticeable when the patient lies down. It varies in size

from time to time and may increase with rise of blood pressure or with tachycardia. There are no local pressure symptoms beyond the throbbing.

Our series comprises forty cases of this condition of kinked carotid, all being women with hypertension or arteriosclerosis or both. In addition, we

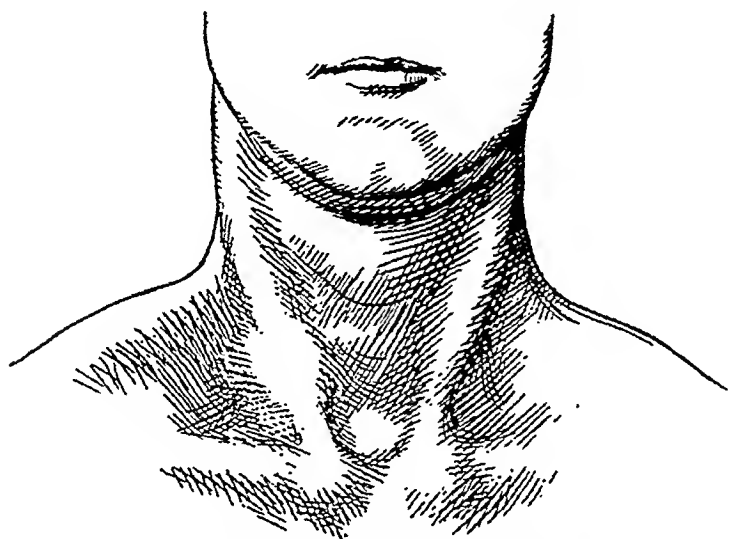


FIG. 2.—Drawing of neck to show a common position of the swelling due to kinked carotid.

have occasionally observed an almost identical vascular swelling in association with aortic incompetence and also with coarctation of the aorta ; these are separately considered.

Group I. With Hypertension or Arteriosclerosis (40 cases)

All were women ; the youngest was aged 41 and the oldest 79, the average being 59 years. The build and appearance were noted in 26 cases, and though 16 of these were obese, 6 were thin. Scoliosis, with the main thoracic convexity to the right and combined with some degree of kyphosis, was almost the rule. Ten of these 40 sought advice solely because of the local pulsation and swelling ; 13 mentioned it in addition to other symptoms.

Hypertension was present in 30 cases (75 per cent.), the blood pressure exceeding 160/95 mm., and in 24 of them the systolic pressure was above 200 mm. In 10 (25 per cent.) the blood pressure was never found raised. Thickening and tortuosity of the radial and brachial arteries were noted in half the cases. None showed evidence of syphilis and in 22 with a recorded Wassermann reaction there was only one positive finding.

There appears to be only one male with kinked carotid on record (Beardwood, 1931) and we also have seen one but have no notes of it. In two of our patients a similar (though less prominent) pulsatile swelling to that on the right was seen in the same position on the left side.

The cardiographic feature was left axis deviation, as would be expected

from the frequency of associated hypertension and a raised diaphragm. Bundle branch block was noted twice and auricular fibrillation twice.

The *X-ray* appearance of the aorta was notable. In 32 cases it was lengthened and uncoiled ; in the remaining 8, 2 were not X-rayed, 4 were inadequately reported, and 2 only showed no abnormality. In 16 the summit of the aorta reached the clavicle and in 2 it extended above the upper border of the clavicle. The heart was commonly enlarged, especially to the left, as expected with hypertension. In a few cases a shadow encroached upon the inner side of the apex of the right lung (Figs. 3 and 4), when it coincided with the area of the pulsating swelling as felt during radioscopy.

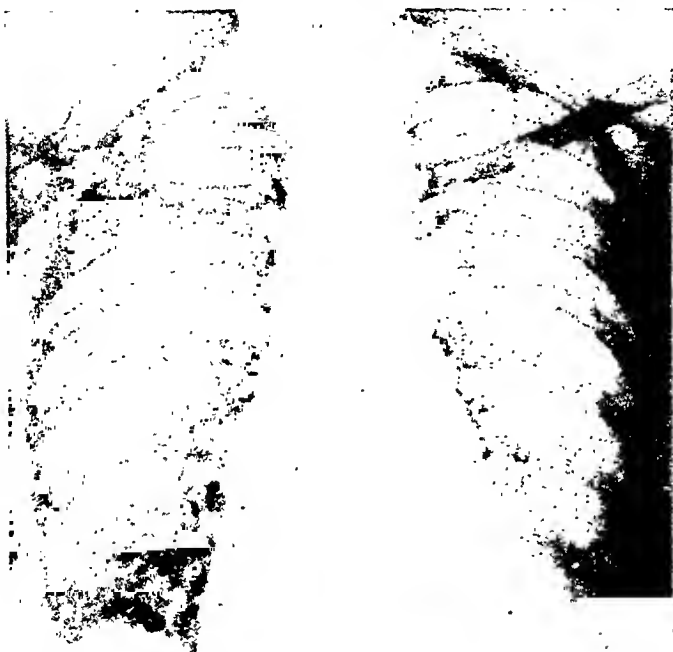


FIG. 3.—Radiograph showing an abnormal shadow at the apex of the right lung due to a kinked carotid. (Case 2 in Appendix.)

The prognosis depends on the cardiovascular disease and is not affected by the presence of a kinked carotid. One patient, first seen in 1923, was alive and well when re-examined fifteen years later at the age of 78. Two others have been under observation for eight and five years respectively, and in several others the swelling had been noted for as long as five to twenty-five years ; even over such long periods there seemed to be little or no increase in the size of the swelling:



FIG. 4.—Radiograph showing a high aortic arch and an abnormal shadow at the apex of the right lung due to a kinked carotid. (Case 4 in Appendix.)

Group II. With Aortic Incompetence (4 cases)

Corrigan (1832) in his original paper *On Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves* stated: "If the arch of the aorta and arteria innominata approach more nearly than usual to the notch of the sternum, the visible pulsation at the root of the neck becomes so prominent as to lead to a supposition that there is aneurysm, and even of considerable size at this part." And again: "So strong were the pulsations for years in the region of the arterio-innominate that until the examination after death there was never even a doubt expressed that the case was not aneurysm."

Hare (1886) reported a girl, aged 17, with rheumatic aortic incompetence "and an egg-shaped protrusion in the suprasternal notch, very expansile and bulging at each systole of the heart"; he considered it to be a small fusiform aneurysm, combined with general dilatation of the aorta and innominate artery. This case is of further interest in that Osler (Osler and McCrae, 1908) personally examined Hare's patient on several occasions and stated: "It was not a case of throbbing of the innominate and the right carotid during ventricular systole, but there was a prominent dilated tumour to be grasped between the fingers just above the sternal notch. . . . At the post-mortem it was not a surprise to find the condition had been one of simple dynamic dilatation."

We have notes of four cases of aortic incompetence in which, besides the

usual carotid throbbing, there was a localized pulsatile swelling at the root of the neck on the right side. The swelling was rather more mesial than was that described as a typical kinked carotid, lying partly in the suprasternal notch and partly behind the right sternomastoid. Here the swelling appeared to be formed by the innominate artery, the origin of which was displaced to the left, so that the vessel crossed the episternal notch from left to right, in front of the trachea. Of our four cases, three were women aged 59, 60, and 67, and one was a man aged 55. All had hypertension and in three the Wassermann reaction was positive.

Group III. With Coarctation of the Aorta (3 cases)

In this congenital anomaly the subclavian arteries are often enlarged and pulsate excessively, but the carotids are not usually affected. We have, however, seen three cases of coarctation with abnormal pulsation in the suprasternal notch or at the root of the neck, not unlike that described under kinked carotid. Two were males, aged 14 and 25, and one was a female, aged 54. The swelling is probably due to elevation and dilatation of the aortic arch and a resultant high bifurcation of the innominate, though another possible explanation is an anomalous origin or course of the vessels springing from the aortic arch. Weber and Price (1912) described a female patient, aged 56, with aortic coarctation, in whom there was "a pulsating aneurysmal swelling on the right side of the neck, in front, just above the clavicle, about the average size of a hen's egg." If coarctation is suspected, confirmatory signs such as the diminutive femoral pulse and the collateral vessels should be sought, and X-rays may reveal an abnormal configuration of the aorta and the characteristic erosive notches on the lower borders of the ribs (Roesler's sign). When a vascular swelling of the root of the neck is found in a male or any young subject with hypertension, in whom the common form of carotid kinking is almost unknown, coarctation is the most likely explanation for it.

Group IV. With Other Congenital Vascular Anomalies

Tortuosity of the internal carotid artery has long been recognized by laryngologists as a developmental abnormality, occurring in the young and often bilaterally. The internal carotid artery originates from the third aortic arch and the dorsal aorta, and at the junction of the two component parts a distinct bend is formed. Kelly (1924) attributed the persistence of undulation or tortuosity to the fact that the normal straightening out of the artery is incomplete. It is manifested by a symptomless pulsating bulge in the lateral part of the pharynx. Kelly reviewed a series of 150 cases which included 21 over the age of 60 (these were believed to be arteriosclerotic) and found that females preponderated. Where the condition was unilateral, it was commoner on the right side.

Freyberger (1898) reported a female patient, aged 26, in whom "a pulsating swelling was visible above the right sterno-clavicular articulation; its centre was covered by the sternal and clavicular insertions of the sterno-mastoid

muscle (the swelling measured $1\frac{1}{2}$ inches from side to side, and about 1 inch from above downwards)." The clinical diagnosis was aneurysm of the innominate artery. At necropsy, the findings were a bulging body caused by an abnormally wide truncus brachiocephalicus into which were inserted the thyroidea ima and left common carotid artery. This short common trunk was in front of the trachea and measured half an inch across. It gave off the right subclavian, right common carotid, thyroidea ima, and left common carotid arteries. The left subclavian artery was in its normal place and position.

ANATOMY, PATHOLOGY, AND CAUSATION

Anatomy

The innominate artery is the first and largest branch of the aortic arch, arising at the level of the upper border of the second right costal cartilage and passing upwards and slightly outwards to bifurcate behind the right sterno-clavicular joint. According to measurements cited by Krause (1868) its usual length is 2.5-5 cm., but in 16 of 219 cases from Quain it exceeded 5 cm. and might even exceed 7 cm. Burns (1809) observed instances of the innominate ascending in front of the trachea well above the top of the sternum before dividing, and mentions a cast in his possession showing the right carotid crossing the trachea two and a quarter inches above the sternum. The right common carotid artery arising from the innominate passes directly upwards in the neck as far as the thyroid cartilage, where it divides to form the external and internal carotid arteries; no branches are given off. Its course is indicated by a line drawn from a point midway between the angle of the jaw and the mastoid process to the sterno-clavicular articulation.

Pathology

Necropsies were obtained in two of our cases summarized below, and in addition we have notes of a third necropsy in which a sketch of the tortuous innominate artery was made.

(1) *Case 37.*—An obese woman, aged 41, admitted with shortness of breath, failing vision, and vomiting. A pulsating vascular swelling occupied the right half of the suprasternal notch and extended to the right beneath the right sterno-mastoid muscle. B.P., 235/140; gallop rhythm; extensive albuminuric retinitis; W.R., negative; blood urea, 455 mg. per 100 c.c. Death two weeks later.

Summary of necropsy. Renal insufficiency. Nephritis repens. Considerable cardiovascular hypertrophy. The carotids upon exposure showed no curvature. The innominate artery measured 1.05 cm. in diameter; the right common carotid, 2 cm. from its origin, 0.65 cm.; and the left 0.6 cm. The subclavian artery was slightly widened just beyond its origin (Fig. 5), but unfortunately its diameter was not recorded and no portion was taken for microscopic section. The heart was removed with the neck organs for the illustration and was not returned for weighing.

Longitudinal sections were taken from the proximal and distal parts of each common carotid artery and from the innominate artery, aortic arch, and abdominal aorta. Paraffin sections were stained with hæmatoxylin and eosin, Weigert's iron hæmatoxylin, and Ponceau S, Weigert's fuchsin, and neutral red for elastic fibres, and thionin according to Hoyer's method for mucin.

In the media of the *proximal portions of the right and left common carotid arteries* the elastic content was normal, the collagenous stroma was slightly increased, and there was mucous degeneration, which for the most part was confined to a zone beneath the intima but in one segment of each artery extended almost to the ad-

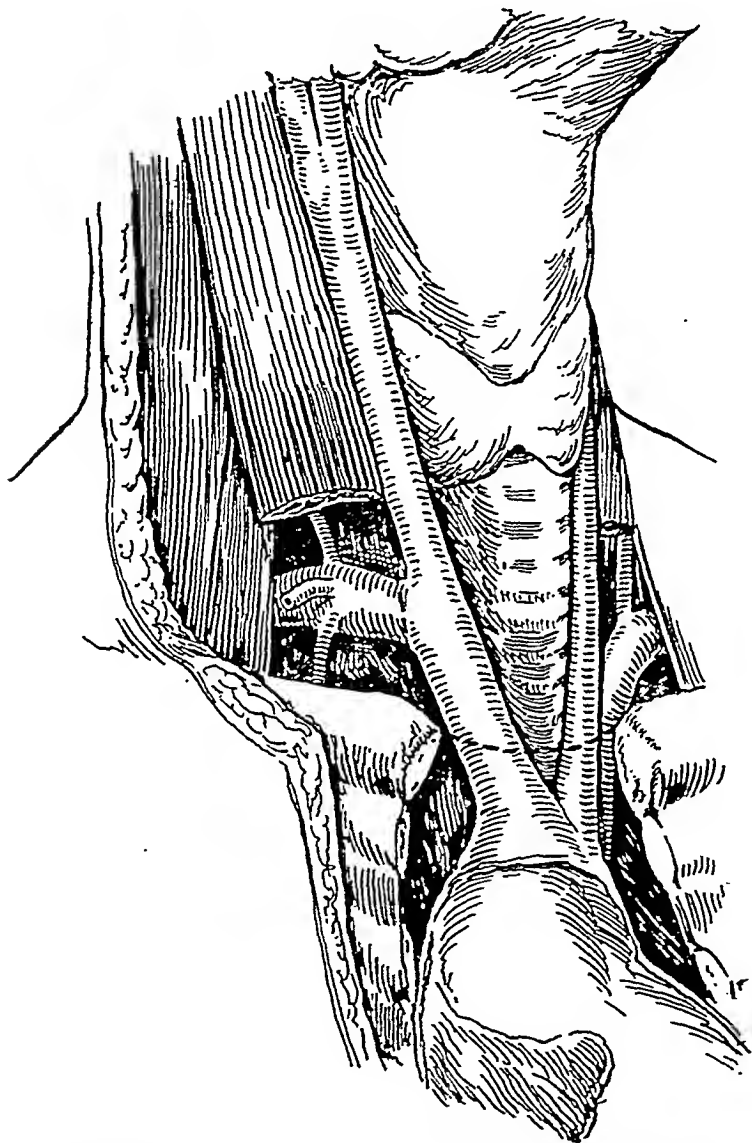


FIG. 5.—Drawing of aorta and great vessels in situ, post mortem, showing high bifurcation of innominate and slight localized dilatation of right subclavian (Case 37). Level of upper border of sternum indicated by dotted line.

ventitia. The degeneration was very slight upon the right side and moderate upon the left. On the other hand intimal hypertrophy was greater on the right side ($1/15$ to $2/3$ of the depth of the media as opposed to $1/13$ to $1/4$ on the left) and showed slightly more degeneration, three small areas of fatty atheroma being present. In the *distal portions* mucous degeneration was greater on the right side and involved

more of the media; it was not, however, severe. Intimal hypertrophy was much greater upon the right side, being from $\frac{3}{4}$ to $\frac{9}{10}$ of the depth of the media as opposed to $\frac{1}{9}$ to $\frac{1}{3}$ on the left. Further, the intima on the right side showed considerable mucous degeneration, while that on the left was free. In the *innominate artery* mucous degeneration of the media was very slight and patchy. In its depth and the amount of degeneration the intima was very similar to that of the proximal part of the left common carotid artery. In the *aorta*, particularly the abdominal portion, medial degeneration was greater than in the above arteries. In the *arch* the elastic was intact but there was a focal fusiform area in the centre of the coat in which muscle fibres were absent. There was considerable mucous degeneration, chiefly in the inner third. The depth of the intima was from $\frac{1}{10}$ to $\frac{2}{7}$ that of the media. In the *abdominal segment* the media was in general narrow, and it was very narrow at one spot where there were small areas in which the elastic fibres were fragmented or absent. There was a little mucus in the inner layers. The depth of the intima was two and a half times that of the very narrow segment of the media and half that of the media elsewhere. It showed much mucous degeneration in its outer part and a considerable number of foam cells.

The degeneration in the arteries was not greater than might be expected in view of the age of the patient and the persistent high blood pressure, which was known to have been present and very high for a year and a half and was doubtless of much longer duration. The degeneration of the media of the proximal portion of the right common carotid artery was not sufficient to have caused an aneurysmal dilatation appreciable clinically. It was, indeed, less than in the corresponding portion of the left artery.

(2) *Case 40*.—Well-nourished woman, aged 43, admitted with a view to operation for "innominate aneurysm." Pulsating swelling in the suprasternal notch and under the right sterno-mastoid muscle in the adjoining supraclavicular region. B.P., 210/140; W.R., negative; blood urea, 285 mg. per 100 c.c. X-ray, great cardiac enlargement and pulmonary congestion. Death a fortnight later.

Pathological summary. Hypertensive failure. Uremia. Myocardial hypertrophy. Severe uræmic changes in kidneys. Terminal suppurative bronchiolitis. Œdema of lungs. Innominate artery branched at about two inches above the right sterno-clavicular joint; no kinking or dilatation noted.

(3) *Case X*.—Male, aged 74, admitted with the clinical diagnosis of hypertension and congestive heart failure.

Necropsy. Heart weighed 14 oz. (397 g.). The aortic arch was dilated and its summit reached the level of the upper borders of the clavicles. The innominate artery was tortuous and dilated, forming a loop which arched across the suprasternal notch from left to right (Fig. 6). The left carotid and subclavian arteries were also tortuous. There was severe kyphosis.

Five published cases with necropsies have already been cited. In Coulson's case the aorta was dilated and elongated and the right common carotid "reduplicated"; in Douglas Powell's case there was atheroma, a high division of the innominate, and a tortuous or bent right common carotid; in Balfour's case there was scoliosis and angulation of the aorta with displacement to the left of the dilated innominate artery, which was two inches long. In Hare's case with aortic incompetence, in which there was an egg-shaped tumour in the suprasternal notch, Osler stated that the condition was one of dynamic dilatation. Finally, in Freyberger's case the vascular swelling proved at necropsy to be a wide and anomalous innominate trunk.

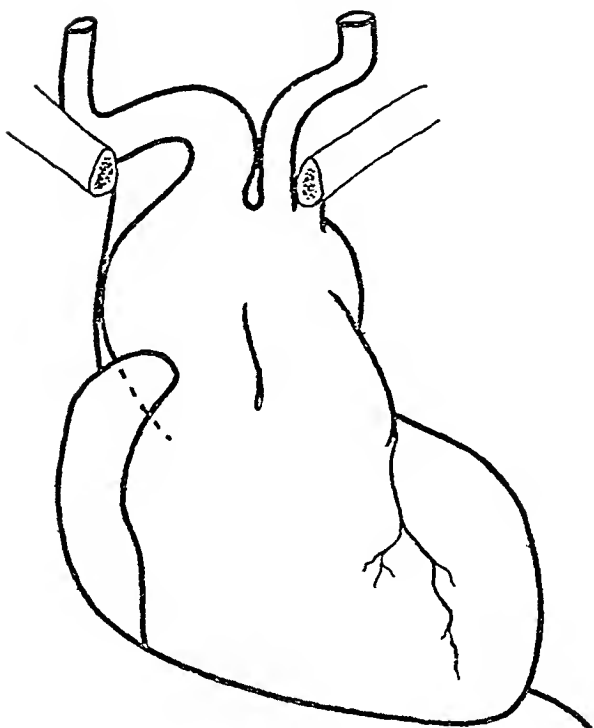


FIG. 6.—Outline drawing of the heart and great vessels in situ from a case of hypertension with kyphosis, showing high, tortuous and somewhat dilated innominate artery.

Causation

Available post-mortem observations show, therefore, that the vascular swelling in question is not due to aneurysm or localized dilatation of an artery, but to a tortuosity either of the right common carotid or of the innominate or of both, together with some degree of general dilatation of these arteries. Elongation and unfolding of the aorta with consequent displacement and elevation of the innominate is usually found. A high bifurcation of the innominate is due either to an unusual length of this artery or to elevation of its origin at the aorta or to both.

The frequency of hypertension is significant. Not only does hypertension produce uncoiling or unfolding of the aortic arch, often with some degree of dilatation, but it also accentuates the dynamic factor. When arteriosclerosis of the aorta is also present, as is usual, there is actual lengthening of the aorta. Thus the aortic arch becomes elevated in relation to the clavicles, and this elevation will be accentuated if the chest is shortened by kyphosis and by the high diaphragm of obesity.

The dynamic factor in these vascular swellings is clearly important, for the bulge seen in life usually disappears after death when the artery is no longer distended under high pressure. A tortuous or looped right carotid or innominate artery will receive direct the full force of a hypertrophied left ventricle, and at each systole an exaggerated movement is imparted to the arterial loop

comparable with that seen in a tortuous brachial artery when the forearm is bent. If aortic incompetence is added to hypertension, this dynamic factor will be reinforced.

As this abnormal pulsation occurs almost exclusively on the right side, an explanation should first be sought in the anatomical differences between the two sides. On the left side the carotid artery is free and has a long course between its origin and the skull, so that any tortuosity might be evenly distributed over its whole length. On the right side, however, the innominate artery and its direct continuation upwards as the carotid artery is anchored quite near the aorta by the right subclavian artery, and therefore elevation of the origin of the innominate will tend to cause a relatively acute kink at the site of the origin of the subclavian. The latter vessel passes backwards and to the right, between the scalene muscles, and any redundant length between the innominate and the fixed part of the subclavian will tend to force the bifurcation of the innominate forwards with each systole. The carotid in addition is relatively fixed at its termination, so that the tortuosity and kinking which form the aneurysm-like swelling lie at the bifurcation of the innominate, particularly at the commencement of the carotid artery, and may involve the adjacent part of the subclavian artery in addition.

The possibility of a congenital factor must be considered in view of the somewhat similar tortuosity of the internal carotid, which has been explained on an embryological basis. In this connection it is interesting to find two pairs of sisters in our forty cases.

To sum up, the vascular swelling consists of an arterial bend or loop in the region of the bifurcation of the innominate artery. It may be composite, and the degree which the carotid itself, the innominate, or even the subclavian artery may contribute to the pulsation is often hard to determine. Even necropsy may fail to reveal its exact nature where the dynamic factor has been predominant in its production.

DIFFERENTIAL DIAGNOSIS

(1) *Carotid Aneurysm*

In a tabulation of 551 published cases of aneurysm involving various arteries by Crisp (1847) the proportion of females to males was less than one to eight; while in the 25 cases of carotid aneurysm there were 13 males to 12 females. Matas (1909) compared the occurrence of aneurysm in the carotid with that in other arteries, and stated that one third of the aneurysms in women occur in the carotid vessels. It is remarked also by Rose and Carless (1937), in reference to carotid aneurysm, that no other external vessel is so frequently the seat of aneurysm in women. Matas also said that the right carotid is more frequently the seat of aneurysm than the left; the points of election are at the origin on the right side, where the carotid is given off from the innominate, and slightly less commonly at its bifurcation. In addition, "carotid aneurysms are usually of small size; they are more often ovoid in form, their long axis lying parallel to that of the vessel."

In a careful search of the clinical records of the London Hospital during the period 1918–38, not a single case of aneurysm of the proximal portion of the right carotid artery was found. There are two specimens of carotid aneurysm in the museum of the Royal College of Surgeons ; one is in the left artery adjoining the aorta, which is also affected by aneurysmal dilatation, and the other is situated at the distal (upper) end of the right carotid where it bifurcates.

A detailed account of 142 cases of aneurysm treated surgically at the Johns Hopkins Hospital has been given by Reid (1926). Included in this number are ten cases (three female) of aneurysm of the common carotid artery, four being situated at the terminal bifurcation of the left vessel. Of the six cases of aneurysm involving the right common carotid artery, three of them lay at the distal (upper) end, whilst of the remaining three, one was continuous with an aneurysm of the innominate artery and the other two were undoubted examples of kinked carotid. One was a female, aged 54, with a history of throbbing in the neck and a systolic blood pressure of 200 mm. At operation no aneurysm was found, the vessel being simply arteriosclerotic. The other case was also a female, aged 46, with no symptoms, but presenting a pulsating swelling in the right side of the neck. The systolic blood pressure was 220 mm., the Wassermann reaction negative, and her arteries were thickened. At operation, no aneurysm was found and it was considered "a case of tortuous sclerotic vessel forced into an S shape."

We are unable to discover a single proven case of isolated aneurysm of the right carotid artery near its origin. The condition must be one of great rarity ; when aneurysm does occur, it is only an extension of an innominate aneurysm—the basic lesion. If, then, aneurysm of the right common carotid is so great a rarity, its frequency as reported in text books and in statistics based on clinical data is fallacious and arises from confusion between aneurysm at this site and kinked carotid. Aneurysm of the right common carotid artery near its origin should therefore not be diagnosed as a separate entity. A pulsating tumour in the right side of the neck in a patient over the age of 40, in the absence of congenital anomalies already discussed, should be considered a kinked carotid, unless it is accompanied by signs and symptoms of pressure on adjacent structures and by radiological or other evidence of involvement of the innominate and aorta.

(2) *Innominate Aneurysm*

Aneurysm of the innominate artery may be present as a small palpable swelling with visible pulsation in the supraclavicular fossa, a fullness above the sternal end of the right clavicle, or a pulsating tumour just above and to the right of the sterno-clavicular joint, spreading characteristically upwards under the sterno-mastoid muscle (Eschenbach, 1923 ; Norris and Landis, 1938 ; Rose and Carless, 1937 ; Parks, 1938).

There are many points of difference from kinked carotid. Innominate aneurysm is three times more common in men than in women (Eschenbach,

1923). Throbbing in the neck is usually associated with pain and dyspnoea and local pressure symptoms—arterial, venous, nervous, tracheal, or œsophageal. The lower border of the swelling cannot be defined, for it extends behind the clavicle. The Wassermann reaction is usually positive and syphilitic involvement of the adjoining aorta is invariable (Warfield, 1935). X-ray examination is usually conclusive, showing a tumour of the superior mediastinum rising on the right side at the upper level of the arch of a dilated aorta (syphilitic) and extending above the inner end of the clavicle. In oblique views, a fusiform shadow originating at the arch of the aorta bulges posteriorly and so causes compression of the trachea—a constant feature (Warfield, 1935). The aortic knuckle is sometimes depressed, whereas in kinked carotid it is high.

The differential diagnosis, therefore, rests on the absence on palpation of a lower limit to the swelling in the neck, a positive Wassermann reaction, the association of pressure symptoms and signs, and the X-ray appearance of the aorta and mediastinum.

(3) *Exaggerated Carotid Pulsation*

Prominent pulsation of the carotid arteries is bilateral in such conditions as neurosis, extreme anæmia, aortic incompetence, and thyrotoxicosis. In hypertension it is frequently right-sided, and of 105 cases of hypertension investigated by Bolotin (1933) 30 per cent. showed pulsation on the right, whereas 24 per cent. had bilateral carotid pulsation, and only 6 per cent. left-sided pulsation alone. This tendency for carotid pulsation to be greater on the right side in hypertension is due in part to those factors that sometimes produce an actual swelling, i.e. kinked carotid.

(4) *Other Conditions: Venous Pulsation*

A dilated jugular bulb occasionally appears as a pulsating sac above the clavicle, especially in tricuspid incompetence. There is also a varix of the right external jugular vein (Hunter, 1927). Goitre affecting the right lobe, especially if cystic, may resemble the condition superficially, as may a cervical rib displacing vessels in the neck. Tumours or enlarged and adherent cervical glands with transmitted impulse may enter into differential diagnosis. Banks-Davis (1924) and Ballance (1924) have both related errors in the diagnosis of a pulsating abscess, especially where an eroded artery has ruptured and given rise to a pulsating hæmatoma or an infected suppurating aneurysm.

SUMMARY

An aneurysm-like swelling on the right side of the neck, the so-called kinked carotid, is described on the basis of 47 cases and a review of the cases published previously.

The common form of kinked carotid is generally associated with hypertension—often with hypertension combined with arteriosclerosis—but sometimes with arteriosclerosis alone (25 per cent.). It occurs in middle-aged and older women, especially in those affected by spinal curvature and obesity, and it is

scarcely ever seen in men. The swelling itself produces no symptoms beyond local throbbing; it changes little if at all in the course of years, and it has no bearing on prognosis. X-ray examination shows elevation of the aortic arch due to lengthening and uncoiling of the aorta, aided by a high diaphragm. Attention is drawn to an abnormal shadow sometimes cast by the kinked carotid, which partly obscures the apex of the right lung.

A comparable vascular swelling may be associated with aortic incompetence, coarctation of the aorta, and other congenital vascular anomalies.

The swelling consists of an arterial prominence with tortuosity in the region of the innominate bifurcation, which is often elevated. It may be formed by a loop of the right carotid, though the innominate itself or even the subclavian may contribute. Atheroma of the aorta and these branches is usually present, but not syphilis. The dynamic factor, accentuated by hypertension, is important in the production of the swelling. The necropsy findings in three cases are reported.

Differential diagnosis is discussed chiefly in reference to aneurysm of the right common carotid artery, for which it is frequently mistaken. The occurrence of isolated aneurysm of the proximal portion of the carotid artery, unless traumatic, is doubted; surgical operations performed for such an aneurysm most often discover no more than a kinked carotid.

We wish to thank especially Dr. Donald Hunter for much help with our early observations and for obtaining the post-mortem drawing in Fig. 5. Dr. R. A. Rowlands, Professor Ellis, Dr. William Evans, Dr. Paul Wood, Dr. Doris Baker and Mr. Pearce Gould kindly gave us permission to investigate and record cases under their care; and Sir James Walton kindly advised us on the surgical aspect. We are indebted to Professor Turnbull for the pathological report on Case 37 and to Professor McIntosh for that on Case 40. The Editor of the *Middlesex Hospital Journal* has permitted the reproduction of Fig. 1.

ILLUSTRATIVE CASES

Group I. With Hypertension or Arteriosclerosis.

Case 1.—Female, aged 52. Sought advice for a lump on the right side of the neck, thought to be gradually increasing in size and noticed for two years.

Examination (1923). A thin and bent patient with a prominent pulsating swelling, the size of a walnut, rounded, beneath right sterno-mastoid muscle, near the sternum, in the position of the right carotid artery. Aneurysm suspected and operation considered.

Course.—In 1927, swelling as in 1923 or larger. Slight left carotid pulsation without any swelling. B.P., 175/75. W.R., negative. X-ray: left ventricle moderately enlarged, aorta unfolded and summit reaches clavicle. Blood pressure: 1928, 140/70; 1929, 135/80; 1930, 155/85. In 1935 death, with hemiplegia.

Case 2.—Female, aged 79. A swelling on the right side of the neck was noted first at hospital in 1913 and again in 1920.

Examination (1938).—Average weight, not stout. Visible pulsation of the right carotid artery at the level of the thyroid cartilage; a little lower down there was a pulsating swelling the size of a pigeon's egg. It extended from the left of the middle of the episternal notch to behind the right sterno-mastoid muscle and then slightly external to it. Its course was upwards and to the right; there was a forward and then a lateral kink before it turned somewhat posteriorly and then upwards to the normal position of the common carotid artery. The swelling was more noticeable on lying

down. Slight general kyphosis ; moderate scoliosis to the right. B.P., 260/105. Radial and brachial arteries consistent with age ; no abnormal tortuosity. W.R., negative. X-ray : left ventricle enlarged ; aorta unfolded and elongated, the summit reaching the lower border of the clavicle. A pulsating, faint shadow continuous with the denser aortic shadow extended upwards from below the right clavicle to the apex of the right lung, which it obscured (Fig. 3). When the patient was turned slightly to the right, it filled the centre of the clear space of the right apex. Palpation confirmed that this was due to the pulsating swelling noted in the neck. The diaphragm was not raised.

Case 3.—Female, aged 64. Referred by her own doctor on account of “ pulsating swelling in the right side of the neck ; I think, an aneurysm.”

Examination (1936).—Expansile swelling, round, size of a walnut, above the right sterno-clavicular joint, in the position of the proximal part of the right common carotid artery. It was visible and palpable both internal and external to the sterno-mastoid muscle, equally prominent lying or standing. High dorsal scoliosis to the right, and considerable kyphosis. B.P., 165/80. Brachial and radial arteries were not unduly thickened nor tortuous. X-ray : left ventricle enlarged ; aorta elongated, the summit reaching the upper border of the left clavicle.

Course.—In 1938, no increase in size of swelling. B.P., 195/100. X-ray : left ventricle enlarged ; elongation of aorta, with summit reaching above the left clavicle.

Case 4.—Female, aged 65. Swelling in the right side of the neck, of five years' duration.

Examination (1932).—Round pulsating swelling above the inner end of the right clavicle, extending from the middle of the suprasternal notch to a point external to the right sterno-mastoid muscle and projecting this muscle. B.P., 280/140. X-ray : left ventricle considerably enlarged ; wide vascular pedicle with elongation of the aorta so that the summit of the aortic knuckle appeared well above the upper border of the left clavicle, obscuring the inner portion of the apex of the left lung. The apex of the right lung was also obscured in its inner half by a shadow with an outward convexity which was shown during radioscopy to be subjacent to the pulsatile vascular swelling in the neck (Fig. 4). The diaphragm was high.

Course.—She died suddenly at home the same year (1932).

Group II. With Aortic Incompetence.

Case 5.—Female, aged 59. History of swelling of the right side of the neck.

Examination (1938).—Pulsating swelling, as large as a hen's egg, above the inner end of the right clavicle ; it projected medially, and its upper and outer portion curved laterally and then medially to attain the normal position of the right common carotid artery. Aortic diastolic murmur ; pulse collapsing ; radial and brachial arteries thickened and moderately tortuous. B.P., 220/60. W.R., positive. X-ray : heart enlarged to the left, aorta elevated and slightly widened.

Group III. With Coarctation of Aorta.

Case 6.—Male, aged 25. Pulsating swelling noticed in the neck for many years.

Examination (1927).—Pulsating swelling in the right side of the neck, situated in the suprasternal notch and also under the right sterno-mastoid muscle. The bifurcation of the innominate artery was palpable above the clavicle, and the right common carotid seemed dilated and tortuous. The pulsating swelling appeared to be caused by the tortuosity of the common carotid. The temporal and external carotid arteries were dilated and tortuous, and pulsated excessively. Loud systolic murmur at the base ; aortic second sound loud and ringing, followed by a short soft aortic diastolic murmur. B.P., 195/85, right arm. Femoral pulse almost absent. X-ray : considerable enlargement of left ventricle ; aortic arch high, ascending aorta much dilated and the pulsation exaggerated.

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